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Complementary and alternative medicine use by cancer patients commencing curative-intent chemotherapy: survey and educational intervention

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Abstract

Aims

The aims of this thesis were to establish to what extent adult cancer patients receiving curative-intent chemotherapy potentially compromise their treatment and/or safety by using complementary and alternative medicine (CAM), and to identify which cancer patients use CAM at this time, why they use it, and who are most at risk. Additionally, it aimed to establish whether there was a need for an educational intervention to guide cancer patients on the safe use of CAM with chemotherapy, develop and publish the educational intervention and to evaluate the effectiveness of the intervention through surveying cancer patients and cancer care professionals, particularly doctors.

Methods

The thesis employed mixed methods, over several phases: a literature review, an observational study of 75 solid tumour patients receiving curative-intent chemotherapy for the first time and then, using results obtained as a framework, an educational brochure intervention was developed. Qualitative methods were used to evaluate the potential acceptance and content of the educational brochure and also to determine the effectiveness of the brochure post publication and intervention.

Results

Patients receiving chemotherapy may be consuming CAM to treat cancer, to lessen chemotherapy side effects, for symptom management, or to treat conditions unrelated to their cancer. Others may influence cancer patients in their CAM decision-making: practitioners, family, friends, spouse and even casual acquaintances met in waiting rooms and support groups. Cancer patients do not necessarily volunteer their CAM consumption unless asked and prefer their cancer doctor to initiate discussions regarding CAM use. Cancer doctors are reluctant to initiate CAM discussions with their patients.

CAM that is systemically absorbed and biologically active is the most likely to interfere with concurrent chemotherapy and potentially cause harm to cancer patients. The curative-intent patient population are most at risk through taking biologically-

active CAM adjuvant with chemotherapy, by altering chemotherapy dose intensity, which may adversely affect disease-free and overall survival. Mind-body CAM, which has no biological activity, has shown efficacy above standard care when used for support by patients receiving chemotherapy and, when applied using reasonable patient specific precautions, is safe to use with adjuvant chemotherapy treatment.

The curative-intent cancer patient study found 60% of the 75 participants were using CAM at the start of chemotherapy treatment. Biologically-active CAM assessed as having potential to interact with prescribed chemotherapy through diminishing dose intensity was ingested by 27% of patients, all of whom had routinely used CAM prior to cancer diagnosis. This was found to be statistically significant (β= +3.13, P = 0.003). CAM was used by 51% of patients for supportive care reasons and by 28% of patients with the intention of treating their cancer. Thirteen percent of patients were told by a CAM advice-giver not to have chemotherapy. The majority of patients (84%) would have liked to receive information on which CAM is safe to use with chemotherapy in a written handout form, before treatment commencement.

Cancer patients receiving chemotherapy reported that the developed and published educational brochure was easy to understand and most (90%, n=30) thought the brochure had enough information to answer their CAM questions. All cancer doctors (100%, n=17) perceived a need for the educational intervention, and recommended the brochure to their patients. All cancer doctors thought the brochure made it easier for them to discuss CAM with their patients.

Discussion

The majority of patients receiving chemotherapy will consider taking CAM at some time during their treatment. If biologically active, this CAM may alter their chemotherapy effectiveness. Cancer patients may be receiving CAM advice to use biologically-active CAM at the time of receiving chemotherapy from uninformed sources and in some circumstances are advised not to proceed with chemotherapy treatment. There can be a communication gap on CAM use between cancer patients and their cancer doctors, as cancer patients are often reluctant to declare their CAM use or intention and prefer their cancer doctor to ask. Evidence-based guidance on the safe use of CAM with chemotherapy is desired by cancer patients and should be

communicated to cancer patients by cancer health professionals to enable patients to make informed decisions on CAM use at that time. The evidence-based CAM-with-chemotherapy patient brochure, developed through this thesis and now in use at adult day cancer care centres in Queensland, may be a useful adjunct for use by cancer doctors and associated cancer health professionals to educate patients on the potential dangers of biologically-active CAM use with chemotherapy and to provide patients with safe CAM alternatives.

Declaration by author

This thesis is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. I have clearly stated the contribution by others to jointly-authored works that I have included in my thesis.

I have clearly stated the contribution of others to my thesis as a whole, including statistical assistance, survey design, data analysis, significant technical procedures, professional editorial advice, and any other original research work used or reported in my thesis. The content of my thesis is the result of work I have carried out since the commencement of my research higher degree candidature and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution. I have clearly stated which parts of my thesis, if any, have been submitted to qualify for another award.

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Publications during candidature

Peer reviewed papers

Smith PJ, Clavarino A, Long J, Steadman KJ. Why do some cancer patients receiving chemotherapy choose to take complementary and alternative medicines and what are the risks? Asia Pacific Journal of Clinical Oncology, 2014; 10: 1-10. doi:10.1111/ajco.12115

Smith PJ, Clavarino AM, Long JE, Steadman KJ. Evaluation of a patient CAM-with-chemotherapy educational brochure. Evidence-Based Complementary and Alternative Medicine, 2015; Article ID 408430, 5 pages. doi:10.1155/2015/408430

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Smith PJ, Clavarino AM, Long JE, Steadman KJ. Evaluation of a patient CAM-with-chemotherapy brochure. The Australasian Pharmaceutical Sciences Association (APSA) 2014 Conference, 5-7 December, 2014. Brisbane, Australia.

Smith PJ, Clavarino AM, Long JE, Steadman KJ. The use of a brochure to enable CAM-with-chemotherapy patient education. European Breast Cancer Conference, 9-11 March, 2016. Amsterdam, Netherlands.

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I wish to acknowledge the hundreds of cancer patients I have met over many years in my work as a cancer pharmacist. Their feedback compelled me to undertake this thesis in the practical way I have, to find and act upon information gained in order to make an academic contribution and to make a difference to the decision-making burden that cancer patients face during the difficult and crucial time of receiving chemotherapy treatment.

Keywords

chemotherapy, complementary and alternative medicine, patient education

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Chapter 1

Introduction

1 Introduction

Complementary and alternative medicine (CAM), an umbrella term found useful in the context of research, policy making and education,[1] is defined as a broad and diverse group of treatments and products that are not widely used by conventional healthcare professions.[2] CAM includes complementary medicine, which are treatments or products that are used alongside conventional medical treatment, and alternative medicine, which are treatments or products used instead of some, or all proffered conventional medical treatment. Most CAM used by patients together with their conventional medical treatment fall into two subgroups, natural products and mind-body practices. Natural products comprise substances such as herbs, vitamins, minerals and probiotics. Mind-body practices are a diverse group of procedures or techniques sometimes administered by a practitioner, such as acupuncture, hypnotherapy, movement therapies, meditation, massage and healing touch.[3]

Natural product CAM may be administered in a variety of ways, as is the case for pharmaceutical drug administration, with oral and topical being the primary routes of administration. However, not all natural product CAM are biologically active. For example, the practice of homeopathy administers natural product CAM in doses so low that biological activity cannot be achieved.[4] The term "biologically active" is used as a descriptor in this thesis and is defined as the inherent capacity of a substance to alter one or more chemical or physiological functions of a cell, tissue, organ or organism. Biological activity may reflect a "domino effect", in which the alteration of one function disrupts the normal activity of one or more other functions.[5]

The majority of cancer patients receiving chemotherapy will consider using CAM at some time during their treatment[6] and, if so, may be compromising their treatment effectiveness, particularly if they are consuming CAM that has biological activity.[7-12] The potential for adverse outcomes associated with taking biologically-active CAM concurrently with chemotherapy is through interactions that may change the efficacy of chemotherapy.[13] By contrast, natural product-derived CAM that has no evidence for biological activity by virtue of their extreme levels of dilution, e.g. homeopathy and Bach or Australian flower remedies, and mind-body CAM, are not generally associated with any concern for interaction with chemotherapy.

Cancer patients who use CAM during chemotherapy treatment are more likely to be women, their motivations for using CAM differ if being treated with curative or palliative intent, and they are likely to be influenced by others in their CAM decisions.[14] Cancer patients receiving chemotherapy may also be contending with pseudoscientific alternative treatment advice, received from family, friends or CAM practitioners, that counters evidence-based information on cancer treatment and outcome expectation.[6,15,16] Patients prefer their health care providers to initiate discussions regarding CAM use and do not necessarily volunteer their CAM consumption unless asked.[11] The paucity of evidence for efficacy and safety for the use of biologically-active CAM during chemotherapy treatment may be countered by the fact that mind–body therapies have evidence for supportive care (above standard care) and may be recommended to patients looking for a complementary approach while receiving chemotherapy.[17]

1.1 Thesis rationale

Though there is much existing information on the general use of CAM by cancer patients, to date there is little published information on CAM use at the time of receiving chemotherapy: what CAM is used at that time, whether CAM taken compromises treatment or safety, or why cancer patients may take CAM with adjuvant chemotherapy. Observations made over many years, as a practising cancer pharmacist interviewing cancer patients, many of whom used CAM, led to a desire for a greater understanding and more knowledge of CAM use adjuvant with chemotherapy. The major thrust of this thesis was to analyse, interpret and then act upon information gained from surveying a sample population of cancer patients receiving curative-intent chemotherapy and from cancer doctors prescribing chemotherapy at the Sunshine Coast Cancer Care Service, Nambour Hospital, Queensland, Australia.

1.2 Thesis approach

The literature review (Chapter 2) did not find any study that exclusively examined CAM use in curative-intent cancer patients, which is a particularly vulnerable population because treatment success relies on appropriate dose intensity to gain optimal outcomes. The major study forming the body of this thesis (Chapter 4) therefore examined a sample population of solid tumour cancer patients attending the

Sunshine Coast Cancer Service Day Unit and receiving curative-intent chemotherapy for the first time. The study investigated patients' CAM selection, their CAM selection influences and whether their ingested biologically-active CAM had the potential to interact with chemotherapy. The study also captured the CAM-with-chemotherapy educational requirements of these patients.

Chapters 5, 6 and 7 outline the development, acceptance and effectiveness of a purpose-designed patient educational brochure on the safe use of CAM with chemotherapy. Chapter 5 discusses the brochure's development, content definition and the steps taken to facilitate publication by the Queensland Government Sunshine Coast Hospital and Health Service. Chapter 6 discusses the draft brochure's pilot evaluation by both cancer doctors and patients and the reasons for any changes. The post-intervention study (Chapter 7) looks at whether the brochure aided discussions between doctors and their patients on the effects of CAM, helped patients understand the potential effects of CAM during their chemotherapy treatment and saved doctor consultation time. The study in Chapter 7 also examined whether the brochure's final content and appearance was acceptable to doctors and patients.

Chapter 8 discusses key results, limitations and conclusions. The appendices contain publications and ethical approvals and exemptions gained to perform each study and to publish findings. The thesis results have been peer reviewed through the process of achieving eight publications in six different international journals, encompassing the Asia-Pacific, European and North American regions.

Chapter 2

Literature review

Content from this chapter has been published as:

Smith PJ, Clavarino A, Long J, Steadman KJ. Why do some cancer patients receiving chemotherapy choose to take complementary and alternative medicines and what are the risks? Asia Pacific Journal of Clinical Oncology 2014; 10: 1-10

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2 Literature review

2.1 Introduction

Complementary and alternative medicine (CAM) encompasses a broad and diverse group of treatments and products that do not tend to be widely used by conventional healthcare professions.[2] The decision to use these forms of treatment by cancer patients may, or may not, be practitioner driven. CAM can be administered through mind-body therapies such as acupuncture, massage and meditation or as natural substances such as herbs, vitamins and minerals that may exert biological activity through systemic absorption. CAM practitioners commonly combine mind–body therapies with biologically-active substances. For example, a Traditional Chinese Medicine (TCM) practitioner may recommend acupuncture and/or biologically active herbs, and naturopaths may combine mind therapies with herbs and dietary supplement recommendations.

Biologically-active CAM that is systemically absorbed is the most likely to interfere with concurrent chemotherapy and potentially cause harm to cancer patients.[7-12] As biologically-active CAM, such as herbal products, are being sought by cancer patients with increasing frequency,[18] conventional providers require an understanding of the CAM selection process to promote open disclosure and provide appropriate guidance and professional support,[19,20] particularly at the time of the patient receiving chemotherapy. This review aims to describe existing literature on the use of CAM by cancer patients receiving chemotherapy, and to identify gaps and issues that need to be addressed.

2.2 Literature search strategy

A database search was conducted to identify peer reviewed original research published from 2000 to 2016 investigating CAM use by cancer patients receiving chemotherapy. The search included the databases Ovid-Medline and Embase, and the limits used for both searches were English, Human and Abstracts. Articles were included if they were on the thesis topic and reported original research findings.

The search subject headings used for the Ovid-Medline search were: exp Complementary Therapies/px, td [Psychology, Trends] AND exp drug therapy/ AND

exp antineoplastic agents/. The keyword headings for the Ovid-Medline search were: (complementary medicine OR complementary therap* OR alternative medicine OR alternative therap* OR natural medicine OR natural therap* OR CAM).ti,ab AND chemotherapy*.ti,ab AND (cancer or tumor or tumour or neoplasm).ti,ab. The search subject headings employed for the Embase search were: 'alternative medicine'/exp AND 'cancer chemotherapy'/exp. The keyword headings used for the Embase search were: (complementary medicine OR complementary therap* OR alternative medicine OR alternative therap* OR natural medicine OR natural therap* OR CAM):ti,ab AND chemotherapy*:ti,ab AND (cancer or tumor or tumour or neoplasm):ti,ab.

The most relevant articles located using the database searches above were used as the basis for two additional search approaches: Google Scholar was used to search for papers citing the article in question, and the reference lists within the publications were assessed for any relevant articles. This approach allowed for the discovery of publications that were not captured by the database searches.

2.3 CAM definition

Prominent research and health organisations and academics have developed a variety of definitions for CAM that are ultimately quite similar in meaning: i.e. treatments and products that do not tend to be widely used by conventional health practitioners.

The Cochrane Collaboration states that CAM is “a broad domain of healing resources that encompasses all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health systems of a particular society or culture in a given historical period.” [21]

The National Center for Complementary and Alternative Medicine (NCCAM) defines CAM as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine”. It is of note that NCCAM has recently changed its name to National Centre for Complementary and Integrative Health (NCCIH) and now uses the term “integrative” in preference to “alternative”.[3]

The term “integrative” or “integrated” medicine or therapy encompasses the use of CAM with conventional medical practice. Definitions include “a system of healthcare that is patient-centred and collaborative, encompassing a diversity of therapeutic options, which includes CAM, that have been found to be safe, effective and informed by available evidence to achieve optimal health and healing”.[1] A British Medical Journal editorial described integrated medicine similarly, as the practising of medicine in a way that selectively incorporates elements of CAM into comprehensive treatment plans alongside solidly orthodox methods of diagnosis and treatment.[22] The term and practice of integrative medicine is controversial and has been criticised as being an ill-conceived concept, promoting the use of unproven or disproven therapies, which is in conflict with the principles of both evidence-based medicine and medical ethics.[23]

The World Health Organisation (WHO) describes CAM as inter-changeable with traditional medicine; “a broad set of health care practices that are not part of that country's own tradition and are not integrated into the dominant health care system.” Traditional medicine CAM is “the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.”[24]

CAM is explained by the British Medical Association as “those forms of treatment which are not widely used by the conventional healthcare professions, and the skills of which are not taught as part of the undergraduate curriculum of conventional medical and paramedical healthcare courses”.[25]

A European research project termed CAM as a variety of different medical systems and therapies based on knowledge, skills and practices derived outside of conventional health care. The group concluded that CAM was mainly used outside conventional health care, but in some European countries, certain treatments were being adopted or adapted by conventional health care.[26]

Most formal definitions describe CAM as treatments and products that are not considered part of conventional medicine, as did academics Zollman and Vickers in

1999: “a group of therapeutic and diagnostic disciplines that exist largely outside the institutions where conventional health care is taught and provided”.[2]

In Western countries, patients often ‘mix and match’ CAM with conventional medicine. For example, in the cancer setting, a cancer patient may receive chemotherapy and associated conventional anti-nausea medications, but may additionally choose to receive acupuncture, which is CAM, to relieve chemotherapy-associated nausea. Or, a cancer patient may receive chemotherapy and decline associated conventional anti-nausea medications in favour of acupuncture (CAM). In this scenario CAM is used as an alternative to relieve chemotherapy-associated nausea and is complementary to conventional chemotherapy.

There can be some crossover of CAM products, for example, vitamin C taken systemically to relieve a cold is considered CAM as there is insufficient scientific evidence to justify its use in this context;[27] however, if vitamin C is taken to treat a condition caused by a deficiency, such as scurvy, it is considered conventional medicine as there is compelling scientific evidence to support this use.[28]

In summary, complementary and alternative medicines (CAM) cover a broad and diverse group of treatments and products that do not tend to be widely used by conventional healthcare professions. This approach to defining CAM by exclusion, i.e. describing CAM through what it isn’t rather than what it is, has been adopted by most prominent research organisations and academics because specific CAM treatments are varied and fluid.[1] However, CAM treatments and products broadly fall into two subcategories. Natural products such as herbs, vitamins and minerals that are consumed orally or applied to the body, which may or may not exhibit a biological effect, and mind-body practices such as acupuncture, hypnotherapy, movement therapies, meditation, massage and healing touch that have no evidence for biological activity.

2.4 Prevalence of CAM use in the general population

The first nationally representative survey in the US regarding the prevalence of CAM use involved a random sample of 1,539 adults who were interviewed by telephone in 1990. The survey reported that one in three respondents had used at least one form of

CAM during the past year to treat their most serious or bothersome medical condition(s). The study also found that CAM was used primarily for chronic conditions, and in addition to rather than as a replacement for conventional medicine. It also found that a majority (72%) of CAM users did not inform their medical doctors that they used CAM.[29] A national follow-up survey found an increase in CAM use by the American public from 33.8 percent in 1990 to 42.1 percent in 1997.[29] This study's findings were supported by another US study conducted through a mail survey of 1,035 randomly selected individuals reporting 40 percent of those responding had used CAM during the previous year.[30]

A 2004 South Australian survey of over 3000 people found CAM was used by 52.2% of the population. The greatest CAM usage was found in women aged 25 to 34 years, with higher income and education levels. CAM providers had been visited by 26.5% of the population and the users of CAM reported a lower quality of life than non-users. More than half (57.2%) of CAM users did not report the use of CAM to their conventional medical doctor.[31] A further 2005 study of a sample of 1067 adults from all Australian states and territories, found 44.1% of those interviewed used some form of CAM. The most common characteristics of CAM users were age of 18 to 34 years, female, employed, well-educated, private health insurance coverage and higher-than-average incomes.[32] A 2010 Australian cross-sectional postal survey sent to a random sample of 4500 Australians aged $\geq$ 50 years found a CAM usage rate of 46.3% and that Australian women used more CAM than did Australian men.[33] A critical review of the predictors of CAM use in Australia over a 14 year period from 2000 to 2014 found a higher rate of use by females compared to males and that Australian female CAM users were more likely to be middle-aged with a higher education and annual income in comparison to female non-CAM users. Australians were found more likely to use CAM to treat chronic conditions, including cancer.[34]

CAM use in Australia is more likely in women with higher income and education levels, and most CAM users also consult conventional medical doctors, though are unlikely to report their CAM use to them. In both the US and Australia, CAM users do not commonly reject all conventional medical care, usually taking a pluralistic approach to illness, with most CAM users also consulting conventional medical doctors. Medical pluralism can be defined as the employment of more than one

medical system or the use of both conventional and CAM treatments for health and illness.[35] It has been suggested that factors influencing medical pluralism, involving non-conventional medical health care such as CAM use, may be attributed to the peculiar attributes of patients such as personality, experience, culture, social class, family, and religion together with individuals' fears, beliefs, behaviour, and the meanings they give to their ill-health which conventional medicine is perceived by the patient to not understand.[36]

2.5 Cancer patient CAM use

Cancer patients, as in the general population, are more likely to take CAM if they have higher education, are female and have higher than average income.[14] The significance of having a higher income has not always been supported in the literature.[8] Age has been found to be a significant factor, although evidence is contradictory.[14] Cancer type, disease progression, fear of recurrence, race, physician dissatisfaction, co-morbidity, higher social status, being married, living in a metropolitan area, normal weight, non-smokers and prior CAM use have been shown to be significant factors for CAM use by cancer patients.[8,37] The majority of CAM studies have been done in the US or other western countries[14] and CAM studies done outside of western countries have not reproduced such consistent results.

An African study on cancer patients showed high CAM use but found women less likely to use CAM than men and that education, income and age were not factors influencing CAM use.[38] A study in Singapore found race, education level and prior CAM use to be significant predictive factors for cancer patients.[39] A Mexican study showed that CAM users were most likely to be higher educated females with advanced cancer.[40] An Iranian study of breast cancer patients found fear of recurrence and dissatisfaction with the physician the most likely causes for CAM use [41] and in Japan, advanced cancer stage, higher education, type of cancer and a younger age were found to influence CAM use.[42]

Men are less likely to take CAM than women.[14] Men who select CAM to treat cancer or to support conventional cancer treatment may not have high regard for scientific evidence and they are most likely to receive their CAM information and motivation from female relatives or friends.[43] Some men with prostate cancer, up to 39% in one

study,[44] used CAM. A US study of prostate cancer patients receiving curative surgery and radiation found a rate of 32% using CAM during treatment[45] and an earlier study on a similar cohort of curative prostate patients measured a rate of 43%.[46] Prostate cancer patients may also use CAM because of disease progression,[47] although it is uncommon for men with any type of cancer to use CAM exclusively without conventional medical interventions.[43]

2.5.1 Australian cancer patients

In Australia, a significant proportion of cancer patients use CAM, with a prevalence measured in a recent study at 65%.[6] The Australian population of cancer patients more likely to use CAM reflects the majority of studies, with these patients possessing higher education, being female and having higher than average income.[6,48] A study on CAM use by elderly Australian women with cancer found that although their CAM use was less than that shown in studies involving women of all ages with cancer, they used CAM more than elderly women without cancer.[49]

Aboriginal Australians are twice as likely to die from cancer as non-aboriginal Australians.[50] Chemotherapy, which may debilitate and take an aboriginal person away from normal societal duties, may be seen as undesirable from an indigenous belief system.[51] Aboriginal Australians would like to use their bush medicines and have these and other traditional healing practices recognised by orthodox medicine.[52] Better cancer outcomes have been shown to occur when traditional aboriginal healing practices (spiritual, physical and emotional) are used with adjuvant conventional interventions to treat cancer.[52 53]

2.5.2 Australian CAM research and educational organisations

Research funding in Australia for independent, rigorous scientific studies on CAM efficacy and safety has traditionally been difficult to obtain. The CAM industry has been hesitant to support research for unpatented herbs because their competitors may benefit as well, and public funding from government organisations has been difficult to acquire as CAM research is contentious and conventional medicine research is prioritised.[54] This situation has been overturned to some extent with the establishment of the National Institute of Complementary Medicine (NICM), based at the University of Western Sydney, and the Australian Research Centre in

Complementary and Integrative Medicine (ARCCIM), part of the Faculty of Health, University of Technology, Sydney, which have attracted industry and Australian government funding to aid their research. Both organisations conduct independent CAM research and provide educational support for health professionals. The NICM examines the safety and efficacy of complementary medicines and the ARCCIM researches CAM use and practice in Australia and overseas. The University of Sydney has accepted industry funding to establish the Maurice Blackmore Chair in Integrative Medicine with the purpose of undertaking CAM research focusing on how CAM may interact with current standard conventional medical treatments.

The National Institute of Integrative Medicine (NIIM) is a not-for-profit organisation involved in CAM teaching and research, and facilitates multidisciplinary clinics utilising conventional and CAM practitioners. The Australasian Integrative Medicine Association (AIMA) is the peak medical body representing the doctors and other health care professionals in Australasia who practise the concept of integrative medicine, combining the use of evidence-based CAM and/or CAM practitioners with orthodox methods of diagnosis and treatment.[22] The practice of integrative medicine has been criticised as merely a rebranding exercise for alternative medicine because CAM lacking in a scientific evidence base, such as chiropractic,[55] is sometimes promoted and practised as integrative medicine.[56] The teaching of integrative medicine in Australian universities has been criticised and cautioned by the Friends of Science in Medicine (FIM),[57] an Australian based organisation committed to maintaining tertiary educational institutions free of health-related courses not based on science.[58]

NPS Medicinewise (known prior to 2009 as the National Prescribing Service) is a not-for-profit organisation whose programs are funded by the Australian government to provide free, independent, evidence-based information on medicines, including CAM, for the benefit of health professionals and consumers.[59] The Cancer Council of Australia provides information specifically aimed at educating cancer patients who are considering using CAM[60] and the Clinical Oncology Society of Australia (COSA) has produced a position statement on the use of CAM by cancer patients that provides guidance for health professionals involved with the treatment of cancer patients who are using or wish to use CAM.[61]

2.5.3 Cancer diagnosis

Cancer diagnosis is a crucial time for CAM decision making by patients. CAM selection decisions have been shown to coincide with conventional medicine decisions.[10] Initial diagnosis and conventional medicine discussions with the treating oncologist are very important. Evidence links increased CAM use to cancer patients who are not satisfied by the initial oncology consultation and proffered options for conventional treatment.[62]

The use of CAM by patients increases after cancer diagnosis,[19 20] in particular, the use of herbal CAM products.[63] Delaying conventional care for the treatment of cancer, through choosing to use only CAM after cancer diagnosis, can worsen patient outcome.[64,65] Cancer diagnosis may cause patients considerable stress, with one Australian study of head and neck cancer patients showing just under one-third (28%) developing post-traumatic stress disorder, [66] which may hinder their decision making and be associated with avoidance of people connected to the cancer experience.[67]

A CAM discussion with an informed healthcare provider, particularly in regard to safety with conventional treatment, should be provided to cancer patients as near to cancer diagnosis as possible.[19] Particular attention should be given to women and higher income individuals at diagnosis, as these populations are the most likely to start CAM at this time.[68] Targeting populations such as these, which are most likely to use CAM, may be a pragmatic way to aim CAM discussion resources within a cancer centre.

2.6 Reasons for CAM use by cancer patients

Cancer patients may be undergoing chemotherapy treatment for palliative reasons to prolong life and lessen cancer disease symptoms, or to treat cancer with curative intent. A Norwegian study found that cancer patients receiving chemotherapy for palliative or curative intent use biologically-active herbal CAM in equal number of products, though palliative patients take them more often.[66] The more frequent use of biologically-active CAM by palliative patients with advanced cancer is linked to a wish to improve quality of life and increase hope for chances of survival.[69] Curative cancer patients tend to use biologically-active CAM to prevent adverse reactions to

their chemotherapy. [66] Men with prostate cancer have been found to use CAM to treat or support themselves after negative experiences with conventional care.[70]

2.6.1 Treat non-cancer conditions

Patients receiving chemotherapy may be using CAM, regularly or occasionally, to treat conditions unrelated to their cancer. For example, an acupuncturist may be sought regularly to treat or prevent migraine. Glucosamine is regularly taken to treat osteoarthritis, and echinacea, which may be purchased at supermarkets, is taken occasionally to treat cold symptoms. A consequence of taking glucosamine or echinacea during cancer treatment is the potential interaction with chemotherapy drugs.[7,71,72]

2.6.2 Support during treatment

Patients receiving chemotherapy may take CAM to lessen chemotherapy side effects or for disease symptom management.[73] Evidence has been established for mind-body CAM to be used safely with chemotherapy for this purpose[74] and is explored further in this review (2.14).

2.6.3 Treat cancer

Some patients receiving chemotherapy take CAM to treat their cancer. Although there are published and ongoing studies on CAM use to treat cancer, definitive evidence to do so is lacking at this time. [11,20] A small proportion of cancer patients, 8% in one study, [75] decide to select CAM alone to treat cancer. Cancer patients who reject conventional treatment, or select CAM initially and delay conventional treatment, potentially sacrifice years of life, particularly if their cancer is being treated with curative-intent. Two studies have found that delayed conventional treatment has a negative impact on breast cancer patients.[65,76]

Cancer patients using CAM are not necessarily hostile to conventional medicine [11] and it is logical for a person suffering from a disease, such as cancer, for which conventional medicine does not have all of the answers, to look to potential CAM benefits. Cancer patients looking for integration would prefer to use CAM through their conventional providers if it were offered, [6] and cancer patients integrating CAM with their conventional care feel they benefit from both.[77]

2.6.4 Improving psychological well-being and control

A British study stated, "Cancer patients receiving CAM reported being emotionally stronger, less anxious, and more hopeful about the future even if the cancer remained unchanged".[78] Cancer patients feel more in control and empowered through CAM consumption,[10,37] though it has been proposed that any perceived benefits cancer patients receive from CAM use are exclusively obtained through the placebo effect.[79]

2.7 CAM safety

Cancer patients who take biologically-active CAM may be compromising their health in a number of ways: through direct adverse effects, potential drug interactions, or by taking poisonous CAM, or CAM that contains toxic contaminants.

2.7.1 Direct adverse effects

Direct adverse effects such as allergic reactions, gastrointestinal complaints, photosensitivity, skin reactions, hepatotoxicity, and neurotoxicity have been reported through herbal CAM use by cancer patients.[11] For example, the herb, black cohosh, which is used to treat menopausal symptoms, has had 30 independent cases of reported hepatoxicity associated with its intake.[80]

2.7.2 Adverse effects due to manufacturing quality

The bioavailability and pharmacological activity of plant-based CAM may vary considerably through differing standards of practice during preparation, [81,82] and some CAM preparations may be contaminated with toxic impurities.[83,84] For example, the herbal combination PC-SPES (PC=Prostate Cancer-SPES= Hope), used to treat prostate cancer, was found to contain varying amounts of synthetic drugs (warfarin, diethylstilboestrol and indomethacin) in addition to the blend of herbal ingredients stated on the label.[85,86] Diethylstilboestrol is a drug that has been used to treat prostate cancer in conventional medicine; however, due to side effects, is rarely used now.[87] It is likely that these products were purposely adulterated, which adds the complication of integrity to herbal research.[88] It has since been proposed that CAM investigators should consider using independent laboratories for quality control evaluations when conducting clinical trials, to ensure integrity of results.[88]

There have also been reports of substitution errors being made in CAM manufacture, including a Chinese medicine case report, where a cancer patient received the wrong herb, *Stephania*, which was substituted for the desired herb, *Aristlochia*. Unfortunately, the patient developed acute nephrotoxicity and later, as a direct result of the error, genitourinary cancer.[89]

2.7.3 Varying distribution of active ingredients within plant tissues

Plant constituents are not always evenly distributed or present throughout the plant. For example, the *Ginkgo biloba* leaf has differing active constituents and differing therapeutic activity from the fruit. In TCM, the ginkgo fruit has been used to treat asthma and bronchitis from as long ago as 2600 BC.[90] Presently, medicines derived from ginkgo leaves are used to improve cognitive function and ginkgo was the most frequently prescribed herbal medicine in Germany for this purpose in 2000.[90] It is therefore important to elucidate detail of plant constituent origin when considering the safety of CAM.

Growing conditions of plants should also be taken into consideration as the concentration of active compounds may vary depending on the location where a plant is grown and the timeliness and conditions of harvesting.[91,92]

2.7.4 Unknown active constituents

Herbal medicine practitioners believe that the original plant tissue is preferable to isolated active constituents. Secondary constituents within the plant are viewed as having a positive role in the absorption, metabolism and excretion of major active constituents.[93] Unknown secondary constituents may be problematic when considering conventional medicine integration because these constituents may also have potential to interact with chemotherapy and be undetected as the cause.[12]

2.7.5 Government regulation of the quality and safety of ingested CAM

The Australian Therapeutic Goods Administration (TGA) has developed a labelling system to identify registered medicines for supply in Australia. Products assessed for safety, quality and effectiveness by the TGA are registered on the Australian Register for Therapeutic Goods (ARTG) and labelled with ‘AUST R’. Medicines must have high-level evidence for efficacy to be registered; very few CAM are registered.

Medicines with low or medium level evidence for efficacy can be assessed by the TGA for listing on the ARTG, and these are labelled with 'AUST L'. Listed medicines are only assessed for safety and quality but not efficacy, and must be a low risk to the public. Almost all biologically-active CAM, such as vitamin, mineral and herbal products, are listed medicines. Some CAM is exempt from regulation by the TGA and so does not carry the AUST L label – these have not been evaluated by the TGA and safety is unknown.[65] This includes products that make a generalised health claim rather than a medicinal claim, and do not look like a medicine, such as teas and nutraceuticals, as well as products that are too dilute to be of concern, such as homeopathic products diluted beyond 5X.[94]

The effectiveness of the TGA's administration of CAM has been questioned in a recent audit report commissioned by the Department of Health and Ageing. The report concluded that the TGA's "light touch" approach to regulating CAM has been a failure and that the regulation of complementary medicines has been of limited effectiveness. The audit noted that up to 90% of complementary products were non-compliant with regulatory requirements and that advertisements making misleading therapeutic claims were going unchallenged. The audit acknowledged that the TGA had limited resources and suggested targeting serial offenders and companies that intentionally try to avoid regulation.[95]

Although the TGA has strategies to provide safe and appropriately labelled biologically-active CAM to the Australian consumer, it is evident at this time that this is not always the case. Those involved in documentation of cancer patients' CAM consumption should be aware of this fact.

2.8 Potential for CAM to interact with chemotherapy

There is indirect evidence for both positive and negative effects of herbal CAM use with chemotherapy; however, currently there is not enough information available about herb-chemotherapy interactions to make definite recommendations.[96] As it has been estimated that herbal CAM interactions are responsible for a substantial number of unexpected toxicities and possible sub-therapeutic treatment seen in cancer patients,[11] this review concentrates on these potential interaction risks for cancer patients.

2.8.1 Herbs

Ingested CAM, particularly herbs, has the potential to interact with chemotherapy drugs. As cancer treatment often produces adverse effects in patients, interactions and any resultant adverse effects of CAM may be hidden, emphasising the importance of knowledge of potential mechanisms of action. It has been estimated that in the population of patients receiving chemotherapy and taking CAM, at least 27% are at risk of a clinically relevant interaction.[97] Some mechanisms of action for biologically-active herbal CAM with chemotherapy have been postulated to occur at an enzyme level, through metabolic pathways or through altering ATP binding cassette transporters.[12] Biologically-active CAM interactions and potential interactions with chemotherapy are less documented than with commonly prescribed drugs;[12] however, some have been studied and further studies are being undertaken.[12,98-101]

Due to the fact that chemotherapy drugs have a narrow therapeutic target range which delineates maximum efficacy and tolerable toxicity, patient chemotherapy doses are carefully calculated by practitioners.[102] The result of interactions with biologically-active CAM may be to render chemotherapy drugs either more toxic or sub-therapeutic, thus compromising treatment.[11] It also potentially skews data from clinical trials if CAM with interaction potential is taken concurrent with a trial drug, but not adjusted for in subsequent analysis.[103]

It has been estimated that approximately one-third of ambulatory cancer patients are at risk of a drug-drug interaction.[104] Adding biologically-active CAM herbal combinations which in turn may have unknown active constituents presents a dilemma when considering safe integration.

2.8.2 Antioxidants

Antioxidant supplementation above normal dietary requirements has been found to be potentially problematic for consumers. Antioxidants decrease the levels of cancer-causing reactive oxygen species (ROS) that are formed during normal metabolism and are therefore sometimes recommended to the general population to reduce cancer risk. However, clinical trials evaluating health benefits of antioxidants have produced conflicting results with some showing an increase in cancer risk associated with

antioxidant supplementation.[105] A large study found that men who took multivitamin supplements more than seven times per week had double the risk of developing fatal prostate cancer compared with men who had never taken multivitamin supplements.[106] A more recent study concluded that supplementation with the antioxidant vitamin E significantly increased the risk of prostate cancer among healthy men,[107] and vitamin E and beta carotene antioxidant supplementation in male smokers has been shown to increase the incidence of lung cancer.[108]

In the cancer setting, two recent studies have shown that antioxidant supplementation accelerates the progression of tumours. Antioxidant supplementation was demonstrated in animal studies to increase the proliferation of human lung cancer cells and tumour growth,[109] and also to increase melanoma metastasis.[110]

Cancer patients are attracted to antioxidant supplements during chemotherapy and a review of studies on antioxidant supplementation to reduce chemotherapy toxicity has found there is some potential.[111] However, it has been proposed that any beneficial effects of antioxidant supplementation to reduce toxicity may be at the cost of diminishing the effectiveness of chemotherapy or radiotherapy by protecting tumour cells from oxidative damage.[73,112-116] Indeed, cancer patients taking supplemental antioxidants to try to reduce side effects of adjuvant radiotherapy in a randomized placebo-controlled trial may have compromised radiation treatment efficacy.[117] The primary mechanism of action of many chemotherapy agents, such as the alkylating agents, anthracyclines, podophyllin derivatives, platinum compounds and camptothecins, is the generation of reactive oxygen species (ROS), which induces apoptosis in cancer cells. Antioxidants may inhibit ROS, thereby protecting the cancer cell from death.[113,114] While a systematic literature review has proposed that no trials provide evidence of significant decreases in chemotherapy efficacy associated with antioxidant supplementation, many of the 19 included studies were small and underpowered, only four studies were double blinded, and presented survival data were premature.[118] Importantly, as most of the included study subjects in this review had advanced or relapsed disease, the results are not applicable to patients with earlier, more chemo-sensitive disease such as the curative population.[118] As there is no conclusive evidence sufficient to produce clinical guidelines on safe

use,[119] antioxidant supplements should be avoided with chemotherapy agents that induce oxidative stress as the mechanism for anticancer activity.

2.9 CAM selection influences

2.9.1 Practitioner recommendation

It has been estimated that adult Australians visit CAM practitioners at the same rate they do medical practitioners.[32] A small proportion of people (6%) visit only CAM practitioners, which suggests that a substantial number of people in the Australian general population who consult a medical practitioner also consult a CAM practitioner.[32] Significantly, many medical practitioners are unaware of their patients' CAM consultations.[32] This has implications for CAM use as cancer patients may be receiving differing points of view from their CAM and medical practitioners.[120]

2.9.1.1 Medical practitioner-recommendation

A study has found that approximately 20% of Australian general practitioners actively practiced at least one form of complementary medicine or therapy, and almost 50% had an interest in CAM training.[121] It has since been proposed that there is a trend for medical practitioners in Australia to incorporate CAM into their practice.[122] Non-CAM medical practitioners are more likely to refer their patients to medical practitioners who practise CAM than to non-medically trained CAM practitioners.[123] Medical practitioners may have varying training and/or education in the use of CAM and, as CAM practice is mostly unregulated, there may be a temptation to stray outside their field of expertise and unethically cross professional boundaries. This was the case when a Queensland general practitioner was suspended from practising for six months in 2011 for administering sodium bicarbonate intravenously, on the advice of a naturopath, to treat a breast cancer patient.[124] Another more extreme example is that of a UK medical practitioner who prescribed and promoted an unproven Indian Ayurvedic herbal blend "Carctol" to treat cancer. The medical practitioner's unsubstantiated endorsements such as ''Since I have been putting people on Carctol I have seen miracles'' appeared in the UK press.[125] No studies can be found to support Carctol's use.[126] The conversion phenomenon has been postulated as a reason medical practitioners become holistic.[127] This is supported by a

study which showed that over half of physicians attending an holistic conference had encountered a spiritual or religious experience.[128]

2.9.1.2 Non-medical practitioner recommendation

Chiropractic, acupuncture, osteopathy, and massage therapy are the most popular provider-based CAM therapies in Australia.[32] Chiropractic, which is the leading CAM therapy choice, does not have robust evidence outside of treating back pain[55,129] and there is a disproportionate lack of evaluation of its safety.[130] One researcher has concluded that the risks of chiropractic treatment by far outweigh its benefit.[131] Though chiropractic is a government-regulated profession in Australia, there has been criticism of the Australian Health Practitioner Regulation Agency (AHPRA) for inaction over complaints made to the board about chiropractic clinic websites that made claims likely to harm consumers.[132]

"External" complementary therapy modalities have little chance of interacting with chemotherapy drugs; however, there are occasions when CAM practitioners may stray out of their expertise. For example, non-medically trained acupuncturists in the UK advised patients about conventionally prescribed medicines, which led in some cases to adverse health consequences for their patients.[133] In 2002, a large proportion of chiropractors in the UK advised parents against the measles-mumps-rubella vaccination for their patients' children.[134]

With the exception of chiropractors, osteopaths and TCM practitioners, CAM practitioners in Australia are not government-regulated professions,[135] although there are a number of voluntary CAM associations.[136] This exemplifies the great variety of education, background and views that may be expressed within each CAM discipline.

Naturopaths, herbalists, TCM practitioners and sometimes chiropractors[137] recommend the use of biologically-active CAM. As naturopaths and western herbal CAM practitioners are not government regulated in Australia, there may be great variation in practitioner quality and practice.[138,139] The variation of standards and levels of training for naturopaths and other CAM providers has given an opportunity for manufacturers of biologically-active CAM, such as herbs and vitamins, to provide unchallenged product information. Practising naturopaths in Australia receive over

90% of their continuing professional education directly from CAM manufacturers and a substantial amount of undergraduate naturopathic education is also supplied directly from CAM manufacturers.[138,140]

Pseudoscience is defined as "claims presented so they seem scientific even though they lack supporting evidence and credibility".[141] The pseudoscience known as "live blood analysis" is practised by many CAM practitioners in Australia; especially naturopaths and sometimes chiropractors, to determine vitamin and mineral deficiencies.[142,143] Unfortunately, general practitioners sometimes use and advertise live blood analysis as part of their clinic services.[144]

Live blood analysis originates from the work of a German researcher Gunther Enderlein, who in 1925 used darkfield microscopy to observe blood phenomena not able to be seen in stained samples. He postulated, among other things, that microbes he observed caused particular illnesses.[145] Enderlein's theory has since been disproven through further microbial and molecular research.[146] A more recent study concluded that live blood analysis is difficult to standardise and diagnostic reliability is low.[145] Further, a specific study looking at cancer diagnosis concluded that live blood analysis cannot reliably detect cancer. [147] Of concern is the fact that live blood analysis apparatus is sold by companies which make and market the minerals and vitamins for which the results of the test are likely to detect deficiencies.[137] Edzard Ernst, Emeritus Professor of Complementary Medicine at the Peninsula Medical School at the Universities of Exeter and Plymouth, described how patients receiving live blood analysis consultations are cheated three times over, *" by being diagnosed a condition they don't have, by being subjected to lengthy and expensive treatment, and by resubmitting to the test to receive news of improvement "*.[148]

Homoeopaths often recommend oral treatment using homoeopathic remedies. As dosages of constituents are infinitesimal,[149] homoeopathy is highly likely to not interfere with chemotherapy. It should be noted; however, that non-medically trained homoeopaths have recommended ''homoeopathic vaccinations'' for which no reliable evidence exists, instead of conventional vaccination.[134]

Pharmacists have been accused of putting profits over professionalism by acting more like shopkeepers who stock products that will sell, rather than have proven ethical health applications.[150] Pharmacists have not always followed ethical instruction from their professional societies in this regard. The Royal Pharmaceutical Society of Great Britain, for example, has raised concerns over pharmacists selling homeopathic products and has called for homoeopathic products in pharmacies to state that there is no scientific evidence to support efficacy beyond placebo.[151]

CAM recommendations may be supplied from uninformed or at least not suitably trained people working in a professional-looking environment. Shop assistants who work in health food stores may take it upon themselves to give unsound CAM advice to patients. A Canadian study found a health food store assistant advising a breast cancer patient to stop her prescribed anti-cancer drug tamoxifen.[152] Pharmacy assistants may have the same potential to give unsound advice and potentially confuse the cancer patient undergoing conventional treatment.

2.9.1.3 Psychopathic practitioner recommendation

Quack health practitioners who promote borderline belief systems in medicine often do so due to having a psychopathic personality.[127] Psychopaths have a cognitive defect which prevents feeling sympathy or remorse. The following psychopathic traits are described by Canadian psychologist, Dr Robert Hare, in his "Psycopath Checklist":[153] lack the capacity to feel compassion, exhibit grandiosity and superficial charm, are pathological liars, employ conning/manipulative behaviour and lack guilt and empathy. The psychopathic traits of grandiosity, superficial charm and pathological lying, when exhibited by a quack practitioner giving cancer patients the very words they want to hear (such as "cancer cure"),[154] can lead the vulnerable patient to believe the rhetoric. Psychopathic health practitioners may range from having no training at all to being among recognised professions such as medical practitioners or dentists.[127]

2.9.2 Non-practitioner recommendation

Most biologically-based CAM is self-selected by patients and influenced from a wide variety of sources and recommendations. An American study showed that the majority of patient use of herbs was for reasons outside of evidence-based

indications.[155] Evidence has been established for certain CAM used in cancer treatment supportive care, for example, ginger, which has been shown to significantly reduce chemotherapy-induced nausea compared with placebo.[156] However, selection data points to the likelihood of cancer patients consuming CAM, with no evidence or even disproven evidence, which may potentially interfere with conventional medicine and cause harm.[155] Non-practitioner based CAM selection is a grey area in the case of patients visiting professional-looking websites, taking online CAM practitioners' advice, and selecting CAM based on that guidance. [157]

Cancer patients may not value scientific evidence[158] and many believe that CAM will benefit their cancer even if studies have not proved efficacy of the CAM selection.[6] In the general population a study found the majority of patients selected CAM outside evidence.[155] Cancer patients may confuse evidence-based CAM with CAM proven to be not efficacious or even dangerous. Flawed CAM, marketed with pseudoscientific assertions, may be very appealing to the cancer patient looking for alternatives. The sheer volume of CAM information may be very confusing to the cancer patient and cause considerable anxiety.[10]

2.9.2.1 Significant others

Cancer patients' decisions for taking CAM are likely to be influenced by significant others: family, friends, spouse, and even casual acquaintances met in waiting rooms and support groups. This influence may range from encouraging and supporting the patient's decision through to making the decisions for the patient.[6,10,16] Men who select CAM to treat or support cancer mainly receive their CAM information and motivation from female relatives or friends.[43] Family and friends who influence cancer patients' CAM decisions feel that the patient does not have the ability to make their own CAM decisions, and can be particularly insistent and persuasive to the patient when they regard themselves as having CAM knowledge or expertise.[16]

2.9.2.2 Media information

Although the internet has many reputable, informative cancer sites, unscrupulous promoters of pseudoscience now have a platform which the uninformed may find seductive.[11,159-161] Additionally, newspaper reports of CAM cancer treatments have been found to mislead.[162] An Australian study found that reports of biologically-

active treatments are the CAM cancer treatments most published in newspapers. Australian newspapers have also been shown to play down potential side effects whilst embellishing potential benefits of CAM, with two-thirds of articles describing CAM use in the context of a cure.[163]

Pseudoscientific CAM options in any media advertising are presented for the layperson, consequently statements and assertions are not referenced. It convinces vulnerable patients by appealing to faith or by promoting fear. Pseudoscience peddlers may be evangelical in their attempts to convert and there is often conflict of interest between the information base and the person promoting it. [141,164] Sellers of pseudoscience may recommend CAM only, and can be very effective at demonising conventional medicine.[161] Some pseudo-scientists may also masquerade as practitioners, practising without qualifications or evidence base.[165] As most cancer patients seeking CAM have expressed a preference to receive it as part of their hospital care,[6] advocates with CAM knowledge are needed within the conventional care setting to at least guide people away from pseudoscience in their CAM choice.[7,10,166]

2.10 Dietary modification

After diagnosis, many cancer patients wish to make dietary modification to include more healthy food choices. Supplemental dietary variations such as vegetable juices often make the patient (and family) feel better and are mainly harmless. It is when the misconception that “diseases can be cured by eating the ‘right’ foods”[167] results in a cancer patient changing their diet to an extreme, such as “carrot juice only”, that dietary modification may be detrimental to the patient’s health. Pseudoscience, misconceptions and myths of the cancer disease process may lead to anxiety-causing statements such as “cancer loves sugar”.[168] Pseudoscience claims such as this can be difficult to counter as it often has some tenuous basis in truth.[169] The saying, "cancer loves sugar" has been around since 1927 when the cell biologist Otto Warburg hypothesised the prime cause of cancer is the replacement of the respiration of oxygen in normal body cells by a fermentation of sugar and this early scientific work is misinterpreted and misquoted as "cancer loves sugar".[168,170] Perhaps another explanation for the persistence in the belief that “cancer loves sugar” is that too much

carbohydrate is consumed in western diets, leading to obesity which is known to be a significant co-morbidity in cancer outcome.[171]

2.11 Spontaneous regression of cancer

Over the last one hundred years, there have been documented reports of spontaneous regression of cancer.[172] Dubious case reports of miracle cures due to CAM do not acknowledge this phenomenon. Although spontaneous regression has been reported in all types of human cancer, the types of cancer most reported were nephroblastoma, renal cell carcinoma, melanoma and lymphoma.[173] Postulated mechanisms of action of spontaneous regression are varied; however, it is agreed that further elucidation would improve cancer treatment.[174]

2.12 The placebo/ nocebo effect

The word placebo originates from the Latin "I shall please," and the placebo effect is often assumed to be only psychological. The placebo effect is, in fact, far more complex and is not constant; differing placebos invoke a greater effect than others for the same condition and patient belief in an intervention produces a greater placebo response.[175] The placebo effect is greater in certain types of diseases and a positive placebo response has been measured in up to 50% of patients suffering depression, pain or Parkinson's disease.[176] Physiological mechanisms of action such as dopamine release (Parkinson's disease) and endogenous opioid release (pain) caused by placebo interventions have been measured.[177,178] The placebo effect becomes greater in proportion to the patient's number of visits and other interactions with health professionals [179] and is also linked to previous positive responses from clinical interventions.[180] More recently it has been found that an individual's response to placebo treatment may be genetically linked. Studies have shown individual genetic variation in the synthesis, signalling and metabolism of the dopaminergic, opioid, cannabinoid, and serotonergic neurotransmitter pathways, contribute to differences in placebo treatment response.[181]

Cancer patients, through belief in a certain CAM and/or CAM practitioner, will experience a placebo benefit whether the intervention works or not, and are not easily swayed by evidence to the contrary.[158] This may be problematic for the cancer specialist, particularly when trying to guide a patient away from potentially harmful

CAM, as patient CAM choices may also dictate engagement with conventional care.[166]

The "nocebo effect" has been described as a phenomenon directly opposite to the placebo effect. A nocebo effect occurs when verbal suggestions of negative outcomes result in a patient expecting and actually experiencing clinical worsening of the condition.[182] It would seem logical that if a cancer patient is told by a significant person that chemotherapy will diminish their cancer outcome, there is a possibility of the nocebo effect worsening that patient's response to chemotherapy.

2.13 Declaration of CAM use to conventional health providers

CAM consumption by cancer patients is often not revealed to their conventional treatment professionals, particularly if the patient is not asked, and many cancer patients who consider CAM to be harmless do not necessarily volunteer use even when they are specifically asked to give this information.[11] Cancer patients would prefer their health care providers to initiate discussions regarding CAM, [15] perhaps due to anticipation of a negative response, in order to avoid risking their relationship with their oncologist. [183] An explanation may be that a neutral or indifferent response may be interpreted wrongly by the patient as a negative response. This indifference may be that the conventional providers view CAM as harmless, at most having only mild interaction potential, and not worthy of consideration.[184] As CAM may interact with chemotherapy leading to adverse effects and potential treatment failure,[97] skilled interview techniques are required. Actively asking, being non-judgemental and explaining potential negative consequences may help extract CAM use information from the patient.[185]

2.14 Obtaining CAM evidence

Evidence-based medicine is defined as the process of systematically reviewing, appraising and using clinical research findings to aid the delivery of optimum clinical care.[186] Conventional research is hypothesis driven, seeking to answer questions of an intervention to a specific symptom or disease, whereas CAM treatment may involve multiple herbs and treatment modalities. It has therefore been suggested that CAM should be studied as a whole and not limited to conventional scientific research.[187] The concept of "black box" study design, which allows traditional CAM practitioners

to use complex modalities to treat patients in a trial [188] has limitations, as outcomes are too broad for meaningful conclusions and may not constitute evidence of scientific value.[187]

Conventional clinical trials normally involve three phases: Phase I looks at safety and dosage on a small population of patients, Phase II trials test efficacy and, in the cancer setting, efficacy for cancer type, and Phase III studies use large numbers of preferably randomized participants to compare the new substance to current standard treatments. There have been very few Phase III trials done on unpatented botanicals due to the complexity and high cost of this level of research.[187] Phase IV studies examine side effects, risks and benefits when the substance is used by a large number of consumers after the treatment has been approved for use.[189]

Using herbs in the cancer setting, either singularly or in combination with conventional treatment, has design challenges when considering safety and appropriate dose. CAM biological treatments often use treatment history as proof of safety; however, this does not constitute safety when used concurrently with chemotherapy.

CAM dose is rarely determined through the conventional trial method of dose escalation[187] and dose response may not be linear. This is the case of the anti-tumour mushroom *Grifola frondosa*, which showed reduced anti-tumour activity at higher dose.[190] The Sloan Kettering Cancer Center researchers have found and published ways to obtain Phase I safety, dosage and efficacy data for botanicals to treat cancer whilst maintaining scientific integrity.[191]

In the cancer setting, the use of a full placebo arm is considered unethical and therefore pragmatic trial methods are used, for example comparing standard care to standard care plus new treatment.[192] Although placebos are unethical to use by themselves in cancer trials, they are still required when using best existing care plus or minus the trial intervention. The formation of an appropriate placebo and blinding of patients is often difficult when trying to measure CAM interventions.[193] Many herbs have distinctive taste, smell and appearance and are hard to duplicate; however,

when volume is not an issue, encapsulation has been used successfully to enable a matching trial placebo.[187,191]

R.B. Bausell, a former Director of Research for the University of Maryland's Centre of Complementary and Alternative Medicine, postulates that all beneficial CAM effects are due to the placebo response.[175] Bausell contends that no methodologically sound CAM studies have been shown to be superior to placebo and that only flawed studies have shown CAM results to be superior to placebo results. In support of this contention, Bausell cites Cochrane Collaboration database studies which found only 5% of ninety-eight legitimate randomised and controlled published CAM studies showed greater than placebo effect.[194-196] There is inherent bias and ignorance of clinical trial methodological issues such as the placebo effect, natural disease history and statistics in clinicians involved in CAM studies. No CAM has scientific validation of mechanism of action beyond that of placebo, and there is a lack of understanding of parsimony, the elimination of variables,[197] leaving the way open in trials for positive effects to be wrongly attributed to CAM.[175]

2.15 CAM with evidence to treat cancer

Anecdotal evidence and encouraging case studies for CAM, as pointed out by Bausell,[175] have not been able to be repeated in more rigorous study settings. When tested in rigorous clinical trials, no CAM cancer treatments alone has shown benefit beyond placebo[175] and the use of CAM concurrently with conventional care has not yet been shown definitively to alter overall survival for the better.[198] There have, however, been some encouraging studies for certain CAM when used as adjuvants with standard cancer interventions to treat cancer. For example, fish oil supplementation was found in a study to increase first-line chemotherapy efficacy in patients with advanced non-small cell lung cancer[199] and polysaccharide K (PSK), a commercial extract of the mushroom *Coriolus versicolor*, has shown promise when used concurrently with chemotherapy to treat leukaemia, colorectal and gastric cancers.[200]

2.16 CAM with evidence for cancer supportive care

Ginger has been shown in a randomized, double-blinded trial to significantly reduce chemotherapy-induced nausea compared with placebo[156] (Table 2.1) but this is the

only biologically-active CAM that has solid evidence for efficacy in cancer patients. Many cancer patients take a variety of biologically-active CAM, especially antioxidants, vitamins and minerals, to try to lessen chemotherapy side effects or to boost immunity; up to 80% of breast cancer women take antioxidants during cancer treatment for this reason.[73] Robust human studies examining which antioxidants should be used, in what specific dose, for which chemotherapy and cancer type, are lacking at this time. As antioxidant supplementation may reduce effectiveness of chemotherapy treatment, and in some circumstances hasten cancer growth and metastasis, they should not be recommended for use by patients receiving chemotherapy.[73]

Table 2.1 Oral CAM with evidence for chemotherapy supportive care

Symptom description	Complementary medicine and evidence	Reference
Chemotherapy-induced nausea	Ginger • Significantly reduced chemotherapy-induced nausea compared with placebo in a randomized, double-blinded trial	156
Chemotherapy-induced diarrhoea	Probiotics/Yoghurt • Decreased fluorouracil chemotherapy-induced diarrhoea without toxicity	201
	• Case report of death in a non-cancer, immune-deficient patient receiving chemotherapy and steroids to treat an autoimmune disease. The patient ate self-selected supermarket yoghurt and succumbed to the *Lactobacillus rhamnosus* probiotic infection.	202
	• Case report of sepsis infection by probiotic lactobacillus acidophilus in a patient with mantle cell lymphoma undergoing hematopoietic stem cell transplant.	203
Cachexia	Fish oil supplement • Provided benefit over standard care to patients with non-small cell lung cancer through maintenance of weight and muscle mass during chemotherapy administration	204

Mind–body CAM can significantly reduce stress, enhance immunity and quality of life, and may increase length of survival for cancer patients[74] (Table 2.2). Mind–body therapy includes relaxation, meditation, imagery, hypnosis, biofeedback, self-

expression, mild exercise, massage and acupuncture. Although study evidence for the efficacy of mind–body therapies has been questioned due to the difficulty of producing, and often the lack of, study placebo controls,[175] benefit over standard care is proven and mind–body CAM therapies are safe to use as adjuvants with chemotherapy.[74] Also, certain mind-body CAM may be received at little or even no cost to the cancer patient, who may be experiencing financial difficulties.[205]

Significant stress has been shown, in an animal study, to stimulate tumour growth through higher levels of cortisol and adrenaline diminishing immune function.[206] Stress is observed more in cancer patients who perceive themselves as helpless victims than those who see the disease as a challenge or opportunity to find what really matters in their lives.[207] Mind-body CAM, which give cancer patients an opportunity to participate in their own care, may alter the patients' view of their cancer to allow them to better deal with the stress cancer diagnosis brings.[74] Cancer patients respond best to individualised mind-body CAM which caters for individual needs and preference.[208]

Integration of massage therapy is advanced and is now an established subspecialty with published integration guidelines and training programs.[209,210] Training of family members in safe and gentle massage may be a cost-effective option for patients and has been studied.[211] Massage therapies which enhance cancer patients' wellbeing are Swedish massage, aromatherapy massage, reflexology, acupressure and manual lymphatic drainage.[212]

Acupuncture, part of TCM, has been practised for thousands of years in China and is defined as the insertion of one, or several, needles into the skin at particular sites called acupuncture points, for therapeutic purposes. Acupuncture points may also be stimulated by variations within acupuncture: moxisbution (heat), acupressure, electroacupuncture and laser acupuncture.[213] Acupuncture is integrated into conventional cancer care at institutions such as Memorial Sloan Kettering Cancer Center and M.D. Anderson Cancer Center.[214]

Table 2.2 Mind–body CAM with evidence for chemotherapy supportive care

Mind–body CAM	Supportive care use	Reference
Acupuncture	• Benefit for chemotherapy-induced acute vomiting	[215]
Acupressure (acupuncture points stimulated by pressure)	• Benefit for chemotherapy-induced nausea and vomiting	[216]
Moxibustion (acupuncture points stimulated by heat)	• Benefit for chemotherapy-induced acute vomiting	[217]
Mild exercise	• Reduces fatigue and enhances life satisfaction	[218] [219]
	• Yoga has been shown to be a useful practice for women recovering from breast cancer treatments to reduce stress, improve quality of life and well-being, and to reduce persistent post-treatment fatigue	[220]
Hypnosis	• Decreased chemotherapy-induced nausea and vomiting	[221]
Imagery and relaxation (e.g. imagining immune cells as powerful medieval knights or big brooms dispatching cancer cells)	• Modulates immune functioning during treatment	[222]
Massage	• Decreased chemotherapy-induced nausea and vomiting	[223]
	• Reflexology decreased anxiety during chemotherapy	[224]
Meditation	• Shown to alter immune patterns by decreasing stress	[225]
	• Decreases anxiety and depression	[226]
Music	• Reduces chemotherapy-induced anxiety	[227,228]
Self-expression (includes written or verbal expression, artwork, humour and movement)	• Written emotional expression has shown a positive effect on outlook and decreased dark feelings in patients with breast cancer	[229]

2.17 Conclusion – where are the gaps in the literature?

There are significant gaps in the literature on CAM efficacy, safety and potential to interact with chemotherapy. Cancer patients may be receiving CAM advice, which is not evidence-based, to use CAM at the time of receiving chemotherapy. Additionally, there is often a communication gap on CAM use between cancer patients and their conventional cancer care providers, especially cancer doctors, as cancer patients are reluctant to declare their CAM use (or intention to use) and expect their cancer doctor to ask them for this information.

Cancer patients' consumption of CAM may vary considerably over the duration of their cancer journey, and consideration is needed on what CAM is taken by cancer patients at the crucial time of receiving chemotherapy. This is particularly the case for patients being treated with curative intent for whom the accuracy of each dose is pivotal in providing treatment efficacy. Beneficial effects of CAM may be attributed to the placebo effect[175] and therefore a better understanding of the potential benefits of the placebo effect may enhance the cancer patient's conventional therapy outcome. Similarly, the nocebo effect should be acknowledged and better understood, as negative comments directed at conventional medicine, if believed by the patient, may lessen the effectiveness of conventional interventions, or lead patients away from conventional medicine altogether. Consideration should be given to how a potentially harmful biologically-active CAM that exhibits a positive placebo effect on a patient may be substituted with either biologically-active CAM with evidence for safety or with safe mind-body CAM to achieve the same beneficial effects. Better understanding of why cancer patients select CAM at this time may prepare conventional professionals to ask the right questions, have appropriate resources and, if needed, to effectively dissuade patients from biologically active CAM that may be detrimental to their treatment.

Chapter 3

Research Questions, Aims, Objectives and Methods

3.1 Research questions

The major research questions addressed in Chapter 4 focus on those people most at risk of compromising a potentially curative treatment, asking:

1. to what extent do adult cancer patients receiving curative-intent chemotherapy potentially compromise their treatment and/or safety by using CAM,
2. who influences adult cancer patients in their decisions to use complementary and alternative medicine (CAM) at the time of receiving chemotherapy,
3. whether there is evidence of a need for an educational intervention to guide cancer patients on the safe use of CAM chemotherapy.

Following on from this, as a suitable educational tool could not be located a brochure was designed as described in Chapter 5 and, using this brochure, Chapter 6 considers the question:

4. To what extent is the potential for medical doctor recommendation and patient acceptance of a purpose designed patient educational brochure on the safe use of CAM with chemotherapy

Finally, following dissemination of the brochure within one hospital cancer facility, Chapter 7 asked the question:

5. To what extent does the availability of a purpose-designed brochure within a cancer service aid doctors' discussions with their patients on CAM use and assist patients to understand the effects of CAM during their chemotherapy treatment?

The major study described in this thesis (Chapter 4) is an observational study of CAM use by cancer patients receiving curative intent chemotherapy for the first time. This is followed by the design and development of an information brochure (Chapter 5) and two quality assurance audit studies conducted during the development of the information brochure educational intervention (Chapter 6) and post-implementation (Chapter 7). All studies were conducted at the Sunshine Coast Cancer Care Services Day Unit, Nambour Hospital, Queensland, Australia. These chapters have been published in peer-reviewed journals, and the methods for each study are contained in

the methods section of Chapters 4, 6 and 7. The section that follows discusses the decisions involved in designing the studies in greater depth than contained in the relevant chapters.

The overarching consideration during study design revolved around the findings of a meta-analysis of 30 years of study surveys of CAM use by cancer patients. This found a variance in results explained by three basic methodological factors; whether the participants were interviewed face-to-face or had self-completed questionnaires, whether participants were provided with predefined lists of different CAM treatments or had to recall them without being prompted, and whether surveys restricted or expanded CAM use to certain CAM categories.[230]

3.2 Chapter 4

Aim

To establish CAM use in a population sample of cancer patients commencing curative-intent chemotherapy.

Objectives

- Measure the number of study participants using CAM at the commencement of chemotherapy treatment.
- Determine whether CAM assessed as having potential to interact with prescribed chemotherapy was used
- Investigate CAM use by patients prior to cancer diagnosis
- Determine whether patients used CAM for supportive care reasons or with the intention of treating their cancer.
- Understand whether patients' CAM decision making was influenced by advice from others
- Consider whether CAM advisers were in favour of chemotherapy treatment.
- Explore patient requirements for educational information on the safe use of CAM with chemotherapy

Methods

A semi-structured interview method was used in preference to a self-completed questionnaire. The self-completed questionnaire mode of data collection has a higher rate of missing responses and also reports a lower percentage of CAM use than interview-based surveys[231] so a semi-structured interview performed at patients' chair-side by the investigator on the day of the patient receiving chemotherapy was thought to assure greater accuracy. The semi-structured interview method, using a trained, motivating interviewer can also increase item response rates, clarify ambiguous questions, and jog respondents' memories for aiding recall of events and behaviour.[230] The semi-structured interview method also enables the interviewer to better record CAM use by study participants, as patients' conception of CAM may sometimes be different from that of health care professionals.[232]

A limitation of the method used in the study in Chapter 4 was that interviewer-guided interviews on CAM may be biased by social desirability. Studies suggest that respondents give more positive and socially desirable responses in interview surveys than in self-administration.[233] For example, study participants may have assumed the interviewer to be in favour of CAM and bias their response accordingly. However, this may not necessarily be the case for cancer patients using CAM, interviewed by a pharmacist, as it could also be argued that within a setting of conventional oncology, respondents are probably less willing to reveal CAM use fearing that this might be regarded as undesirable.[230] With reference to this phenomenon, participants were informed through the patient consent form (Appendix A) and during interview that their study participation, and the findings on their CAM use, had absolutely no impact on their subsequent treatment or interaction with the cancer centre.

Studies using a self-completed questionnaire to survey CAM use by cancer patients report a higher rate of CAM use when participants choose CAM treatments from a presented or prompted list rather than with free recall.[230] This is consistent with questionnaire design on the recall of pharmacological treatments.[234] Surveys that restrict CAM use to certain categories or treatments yield lower prevalence estimates[235] and studies that include prayer as CAM substantially increase the CAM usage rate.[236] It was therefore decided to perform the study using a semi-structured

interview method using a constructed questionnaire (Appendix B) that contained prompt lists from the standard clinical pharmacy medication history list (Appendix C) and a list developed from previous CAM research studies (Appendix B). Prayer was excluded as CAM.

The study in Chapter 4 was approved for commencement by Queensland Government Human Research Ethics Committee, The Prince Charles Hospital (Appendix D) and The University of Queensland School of Pharmacy Ethics Committee (Appendix E). National Low Risk Ethics Single Site Approval and local hospital governance approval was granted after signing of a legal agreement between the Sunshine Coast Hospital and Health Service and The University of Queensland (Appendix F).

3.3 Chapters 6 and 7

Quality assurance audit studies were conducted during the development of the information brochure educational intervention (Chapter 6) and post-implementation (Chapter 7).

Aims

Chapter 6: To investigate, using study samples of chemotherapy prescribers and patients receiving chemotherapy, key aspects of recommendation, content choice and acceptance of a purpose designed patient educational brochure on the safe use of CAM with chemotherapy.

Chapter 7: To establish whether a purpose-designed educational tool used within a cancer service aided doctors' discussions with their patients on CAM use and assisted patients to understand the effects of CAM during their chemotherapy including safe use.

Objectives

Chapter 6:

- Determine cancer care doctors' perception of the brochure's need, potential recommendation and to which patient group/s

- Explore whether cancer patients receiving chemotherapy accept the educational interventional intervention information as relevant, easy to read and understand and whether it answered their CAM questions

Chapter 7:

- Determine whether cancer care doctors perceived a need for the patient educational tool, and recommended the brochure to their patients
- Investigate whether doctors thought the brochure made it easier for them to discuss CAM with their patients
- Consider whether doctors believed that the intervention saved them time during patient consultations
- Explore whether cancer patients thought the brochure had enough information to answer their CAM questions
- Examine whether patients thought the information was easy to read and understand

Methods

The studies in Chapters 6 and 7 assess the patient educational brochure intervention document work up (Appendix G) and post publication (Appendix H) implementation respectively. These studies both contain two study participant population samples, health professionals and cancer patients, who were recruited to the study in the same way. All prescribers of chemotherapy at the Sunshine Coast Cancer Care Services Day Unit, Nambour Hospital, Queensland, Australia were asked to participate, and consecutive cancer patients attending the unit were asked to participate. One prescriber was excluded as he was a collaborator in this research. As both studies were conducted at a single site, they have the limitation that cancer patients attending, and cancer doctors practising, at the Sunshine Coast Cancer Care Service may not be representative of patients and cancer consultants at other sites. Indeed, Nambour hospital treats patients living on the Sunshine Coast of Queensland which is recognised to have a disproportionate population of alternative-thinking people as, in 2012–13, the Sunshine Coast recorded the highest percentage of conscientious objection to vaccination in Australia for children aged 5 years, at 7.1%.[237]

Quantitative survey research methods were used in both studies, focusing on the collection and analysis of subjective data gained in the form of opinions self-reported in questionnaires by study participants. While evidence from survey research is not as inherently strong as evidence from experimental research,[238] this method was adopted for the studies in Chapters 6 and 7 to obtain meaningful quantitative assessments of subjective factors. Another option may have been to use qualitative research methods through, for example, gathering cancer patient participants together in groups, or as one-on-one interviews either in person or via the telephone, to discuss , develop and extract thoughts from narrative explanations.[238] The reason a qualitative approach was not adopted was for pragmatic reasons. Prescribers are inherently extremely busy and so are difficult to schedule at a given time, so a tick and flick questionnaire to complete when they could and then to follow up, was felt most likely to ensure maximum participation and compliance with the return of their answers. Similarly, a distributed questionnaire was thought most appropriate for patients due to them receiving chemotherapy treatment and having to contend with other associated medical interventions and appointments.

For cancer patient participants in both studies, a self-completed questionnaire mode of data collection was used, in the form of a validated Health Service consumer testing feedback form (Appendix I). The form was distributed to patient participants and they were given the option of either completing the feedback form at the day unit or returning the form by mail using a supplied prepaid envelope. For the health professional chemotherapy prescriber participants in both studies, a self-completed questionnaire mode of data collection was adopted, using questionnaires designed to obtain data that met the studies' aims (Appendices J and K). The questionnaire was distributed to staff participants and asked to return the completed form to the investigator personally, through postal mail or through email attachment.

The Chapter 6 study was granted ethics exemption for publication by the Queensland Government Human Research Ethics Committee, The Prince Charles Hospital (Appendix L) and the Chapter 7 study was granted ethics exemption for publication by Queensland Government Human Research Ethics Committee, The Prince Charles Hospital and The University of Queensland School of Pharmacy Ethics Committee (Appendices M and N).

Chapter 4
Complementary and alternative medicine use by patients receiving curative-intent chemotherapy

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4 Complementary and alternative medicine use by patients receiving curative-intent chemotherapy

Abstract

***Aim*:** To determine which types of complementary and alternative medicine (CAM) are being used by cancer patients commencing curative-intent chemotherapy, whether the CAM taken has the potential to affect treatment efficacy, the reasons for patients' decisions to use CAM and whether these patients would like information on CAM safety with chemotherapy.

***Methods*:** 75 solid tumour malignancy patients receiving curative-intent treatment attending a cancer care day unit were interviewed about their CAM use on the day of receiving their first dose of chemotherapy.

***Results*:** 60% of study participants were using CAM at the start of chemotherapy treatment. Biologically active CAM assessed as having potential to interact with prescribed chemotherapy was ingested by 27% of patients, all of whom had routinely used CAM prior to cancer diagnosis. CAM was used by 51% of patients for supportive care reasons and by 28% of patients with the intention of treating their cancer. Patients' CAM decision-making was influenced by advice from family and friends, practitioners, and from casual acquaintances. 13% of patients were told by a CAM advice-giver not to have chemotherapy. The majority of patients (84%) would have liked to receive information on which CAM is safe to use with chemotherapy before treatment commenced.

***Conclusion*:** Patients being treated with curative intent, particularly those with a history of CAM use, may be taking biologically-active CAM with potential to compromise their chemotherapy treatment. These patients want cancer-care health professionals to provide them evidence-based information on safe CAM use with chemotherapy and may be contending with alternative health advice to not have chemotherapy.

4.1 Introduction

Complementary and alternative medicine (CAM) is defined as a broad and diverse group of treatments and products that are not widely used by conventional healthcare professions.[78] CAM includes mind-body medicine such as meditation, massage and acupuncture, and biologically-active products such as herbs and vitamin supplements. Cancer patients, as in the general population, are most likely to use CAM if they have higher education, are female and have higher than average income.[239] The majority of patients receiving chemotherapy will consider using CAM,[6] and are likely to be receiving CAM advice from a variety of sources who may be particularly insistent and persuasive when they regard themselves as having CAM expertise, including family, friends, practitioners and even casual acquaintances.[6,15,16] Many cancer patients take biologically-active CAM such as antioxidants with the intention of lessening side effects from chemotherapy or to "boost" immunity, with up to 80% of women with breast cancer taking antioxidants during cancer treatment,[73] and curative-intent patients may take herbal CAM in the hope of preventing adverse side-effects from their chemotherapy.[66] In Australia, a significant proportion of cancer patients use at least one form of CAM, more often biologically based, with overall prevalence measured at 65%.[6]

Curative treatment of most tumour types is based on the administration of multiple cycles of regularly scheduled chemotherapy. Chemotherapy dose intensity, a function of dose and frequency of administration, has been shown to correlate with outcome for various tumour types in prospective clinical studies.[240] For this reason, granulocyte-colony stimulating factor support is standard treatment in most curative treatments of breast cancer as it enables dose intensity to be kept constant, which significantly improves disease-free and overall survival.[241] Conversely, anything that compromises dose intensity may reduce chemotherapy effectiveness. Orally ingested herbal CAM may be able to affect cytochrome P450 enzymes and drug transporters which are involved in the metabolism of many anticancer drugs, and herbal CAM interactions with chemotherapy have been suggested to be responsible for a substantial number of unexpected toxicities and under-treatment seen in cancer patients.[11,12] Few clinical studies have been performed to elucidate the effects of herbal CAM on the pharmacokinetics of anticancer drugs, and potential interactions are difficult to calculate as herbal supplements are often taken as complex mixtures of

biologically active constituents.[13] For these reasons, it has been proposed that herbal CAM should be considered contraindicated for use by patients undergoing active treatment with conventional chemotherapeutic agents.[116] Antioxidants are another group of products that are commonly used by cancer patients, but it has been proposed that any beneficial effects of antioxidant supplementation to reduce toxicity[111] may be at the cost of diminishing the effectiveness of chemotherapy or radiotherapy by protecting tumour cells from oxidative damage.[73,112-116] Indeed, cancer patients taking supplemental antioxidants to try to reduce side effects of adjuvant radiotherapy in a randomized placebo-controlled trial may have compromised radiation treatment efficacy.[117] The primary mechanism of action of many chemotherapy agents, such as the alkylating agents, anthracyclines, podophyllin derivatives, platinum compounds and camptothecins, is the generation of reactive oxygen species (ROS), which induces apoptosis in cancer cells; antioxidants may inhibit ROS, thereby protecting the cancer cell from death.[113,114] While a systematic literature review has proposed that no trials provide evidence of significant decreases in chemotherapy efficacy associated with antioxidant supplementation, most of the subjects had advanced or relapsed disease so this review is not applicable to patients with earlier, more chemo-sensitive disease such as in the curative population.[118] To date, there is not sufficient evidence to determine whether antioxidants exert a positive or a negative effect with adjuvant cancer treatment.[242] As there is no conclusive evidence sufficient to produce clinical guidelines on safe use,[119] antioxidant supplements should be avoided with chemotherapy agents that induce oxidative stress as the mechanism for anticancer activity.

Considering the narrow therapeutic window of anticancer drugs, relatively small changes in dose intensity due to antioxidant activity or herbal interactions may compromise treatment effectiveness. This is especially important in the curative-intent patient population, as diminishment of chemotherapy dose may reduce effective dose intensity and hence adversely affect disease-free and overall survival. This study aimed to elucidate which CAM are being used in a study sample of cancer patients entering curative-intent chemotherapy treatment, the influences on their decisions to use CAM and to identify, using the literature available, CAM taken which may compromise chemotherapy treatment.

4.2 Methods

4.2.1 Participants

The study was conducted during the 12 month period from March 2013 to February 2014, using adult patients attending the Sunshine Coast Cancer Care Services Day Unit. To be eligible for the study, patients were diagnosed with a solid tumour malignancy and were receiving their first chemotherapy with curative intent. Patients were excluded if they had previously commenced curative-intent chemotherapy elsewhere or were under 18 years of age. Consecutive eligible patients were asked to participate in this study over the 12 month time period. 75 patients were eligible and agreed to participate. One eligible patient (female, breast cancer) declined the study. 19 eligible patients (14 female and 5 male; 12 breast, 5 colorectal, 1 testicular and 1 oesophageal) were missed due to interviewer leave (Figure 4.1). Each patient took part in the interview with the cancer pharmacist investigator immediately before chemotherapy administration and all patients gave written informed consent. The study was approved by Human Research Ethics Committees at Queensland Health (The Prince Charles Hospital) and The University of Queensland. A legal project agreement was signed between the Sunshine Coast Hospital and Health Service and The University of Queensland as a requirement for local hospital governance approval.

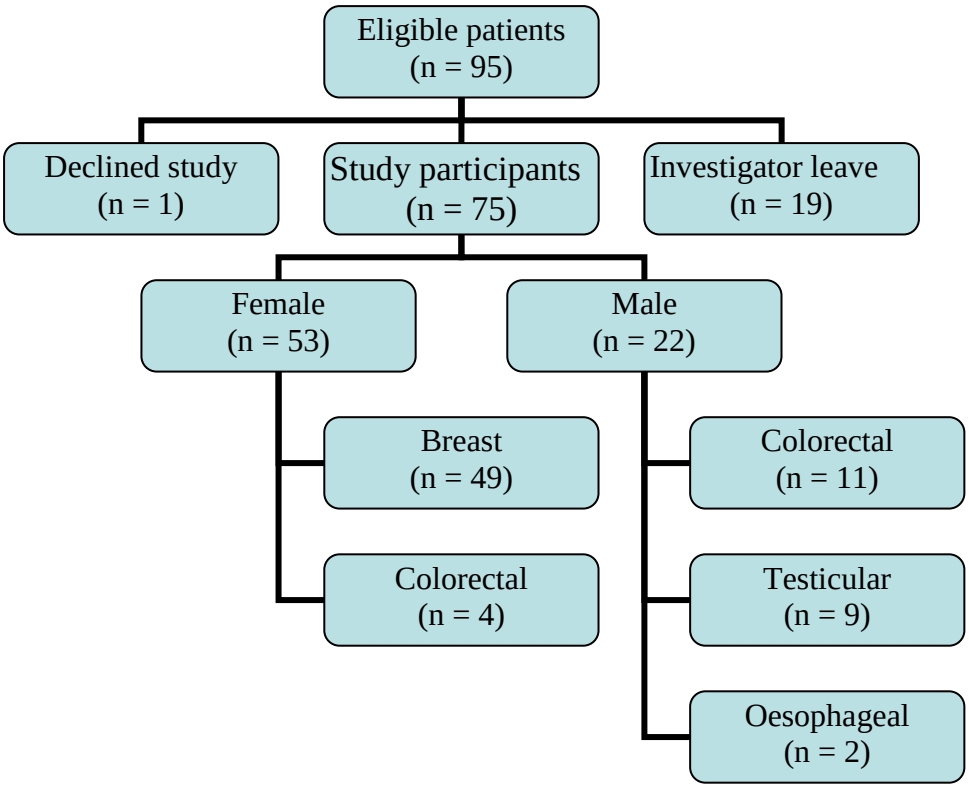

Figure 4.1: Patient recruitment during study period

4.2.2 Interview procedure

A purpose-designed interview guideline was developed based on previous literature to enable semi-structured patient interviews. Questions identified participants' socio-demographic background (including marital status, household gross income, and educational level), previous CAM use and frequency, current CAM use (including ingested CAM use documented as part of the standard clinical pharmacy medication history service for day patients), CAM use declaration to conventional cancer health professionals, expected benefits from CAM use, side effect expectation from CAM use and source of influence on the CAM selected for use. Study participants were asked whether the person giving CAM selection advice was in favour of them receiving chemotherapy. Study participants were also asked whether they wished to receive information on which CAM is safe to use with chemotherapy. Information regarding participants' cancer type and stage, chemotherapy treatment, co-morbidities and any concurrent conventional cancer treatment information was obtained from existing hospital treatment records.

4.2.3 Statistical methods

The data were organised and where appropriate, trends were reported using simple descriptive statistics (mean (SD), median (IRQ) or proportions). Continuous data were checked for normality using the Shapiro-Wilk test. Binary comparisons were undertaken using either a standard unpaired t-test for normally distributed data or a Mann Whitney U-test for unpaired non-parametric or non-normal data. One way ANOVA was used where three or more subgroups were present. Logistic regression was employed to examine the relationship between the explanatory variable current CAM use and the predictor variables age, sex, marital status, educational standard, gross income, malignancy, tumour stage, the presence or otherwise of co-morbid disease and the prior use of CAM. A backwards elimination model was employed and interaction terms were inserted where necessary. The significant results were expressed as the regression coefficient (β) and the associated P-value.
Statistical analysis was performed using a propriety statistical package (STATA version 12.0) and the level of significance was taken as $P < 0.05$ throughout.

4.3 Results

4.3.1 Patient characteristics

The majority of patients interviewed were female (71%) and breast was the most prevalent cancer type (65%), with 71% having a stage 1 or 2 cancer. Ages ranged from 22 to 82 years with a mean of 54 and median of 55 years, 56% were married and 71% had completed education at high school level or above. There were a significantly higher proportion of females, married and high income participants in the CAM use group (Table 4.1).

Table 4.1 Demographic and clinical characteristics for all study patients and for those who used some form of complementary and alternative medicine (CAM) at the time of commencing chemotherapy treatment and those who did not.

Characteristic	n	No CAM use (%)	CAM use (%)	P-value
Total	75	30 (40.0)	45 (60.0)	
Prior CAM use				<0.001
yes	44	9 (30.0)	35 (77.8)	
no	31	21 (70.0)	10 (22.2)	
Age (years) #		56.4 (12.5)	52.9 (11.4)	0.21
20-29	1	0	1	
30-39	8	2	6	
40-49	19	8	11	
50-59	21	10	11	
60-69	20	7	13	
70-79	5	2	3	
80-89	1	1	0	
Sex				0.03
Female	53	17(56.7)	36(80.0)	
Male	22	13 (43.3)	9 (20.0)	
Marital status				0.02
Married	42	13 (43.3)	29 (64.4)	
Defacto	7	1 (3.3)	6 (13.3)	
Single	26	16 (53.3)	10 (22.2)	
Highest Education				0.08
Primary	7	4 (13.3)	3 (6.7)	
Secondary year 10	14	8 (26.7)	6 (13.3)	
Secondary	30	11 (36.7)	19 (42.2)	
Secondary + TAFE	8	3 (10.0)	5 (11.1)	
Tertiary	14	3 (10.0)	11 (24.4)	
Post grad	2	1 (3.3)	1 (2.2)	
Household income (gross, AUD)				0.001
0-30	29	18 (60.0)	11 (24.4)	
31-59	22	8 (26.7)	14 (31.1)	
60-100	9	2 (6.7)	7 (15.6)	
Over 100	15	2 (6.7)	13 (28.9)	
Malignancy				0.29
Breast	49	16 (53.3)	33 (73.3)	
Colorectal	17	9 (30.0)	6 (13.3)	
Oesophageal	2	1 (3.3)	1 (2.2)	
Testicular	7	4 (13.3)	5 (11.1)	
Tumour Stage				0.34
I	14	7 (23.3)	7 (15.6)	
II	39	10 (33.3)	29 (64.4)	
III	22	13 (43.3)	9 (20.0)	
Co-morbidities				0.59
yes	45	18(60.0)	27 (60.0)	
no	30	12 (40.0)	18 (40.0)	

Age was normally distributed and is presented as mean (SD).

4.3.2 CAM use with chemotherapy

60% (45/75) of study participants engaged in CAM use at the time of commencing chemotherapy treatment, of which most (41/45) orally ingested CAM (Table 4.2). Two variables were identified as significant to CAM use with chemotherapy: income ($\beta = +0.76$, $P = 0.007$) and routine prior use of CAM ($\beta = +2.01$, $P < 0.001$). Patients ingesting CAM when starting chemotherapy consumed between 1 and 15 different CAM products with a median of 3 and mean of 4 products taken per patient. Mind-body CAM such as massage, meditation and acupuncture was used by 29% of all study patients for support (Table 4.2). Only one patient expected to experience side-effects from CAM use and this was weight loss through dietary alteration.

Table 4.2 The number (and %) of patients using orally ingested and mind-body CAM at the time of commencing chemotherapy treatment, with potential effect or interaction indicated for each type based on information in the literature.

Type of CAM	Number (%) of patients	Comment
Orally ingested CAM (n = 41)		
vitamin supplements	23 (56%)	potential decrease in therapeutic response [112]
mineral supplements	19 (46%)	-
herbal products	14 (34%)	potential for interaction [11,13]
fish/krill oil	13 (32%)	potential chemo-resistance effect [243]
probiotics	10 (24%)	-
CoQ10	7 (17%)	potential decrease in therapeutic response [112]
turmeric	6 (15%)	potential decrease in therapeutic response [244]
medicinal mushrooms	4 (10%)	-
ginger	3 (7%)	may reduce chemotherapy-induced nausea [156]
homeopathic preparations	3 (7%)	-
glutamine	2 (5%)	-
apricot kernels	2 (5%)	potentially toxic [245]
other: lemon/ sodium bicarbonate/ proprietary “alkaline” water, diluted sodium chlorite	7 (17%)	-
Mind-body CAM (n = 22)		
massage/ reflexology†	14 (64%)	†benefit over standard care for chemotherapy treatment support [17,246]
meditation†	7 (32%)	
acupuncture/acupressure†	4 (14%)	
yoga†	1	
aromatherapy	4 (14%)	
crystal healing	2	
bowen therapy	1	
reiki	1	

Supplementary vitamins were taken for reasons other than treating a medical deficiency by 23 patients. Of these, 3 patients took a single standard multivitamin daily for non-cancer reasons without further supplementation; as in previous studies[116,247,248] these patients were not assessed as having chemotherapy interaction potential, although any supplementation above normal dietary intake should be regarded with suspicion until further research proves safety.[114] The other 20 patients (16 female, 4 male) were taking antioxidant supplements (vitamins A, C, E, beta carotene and coenzyme Q10) with potential to diminish their prescribed chemotherapy effect by protecting tumour cells from oxidative damage.[112] All 20 patients were taking antioxidant supplements with chemotherapy agents that induce oxidative stress for anticancer activity: alkylating agents, anthracyclines, podophyllin derivatives, and/or platinum compounds[114] (Table 4.3).

Table 4.3 The study patients who were at risk of diminished effectiveness of their chemotherapy through taking oral antioxidant supplements at the same time

Cancer type	F	M	Stage l	Stage ll	Stage lll	Chemotherapy treatment	Chemotherapy with potential for diminished dose intensity from antioxidant supplementation
Breast	4	-	1	3	-	AC; 4 cycles (+/- paclitaxel x 12)	cyclophosphamide, doxorubicin
Breast	4	-	1	3	-	TC 4 cycles	cyclophosphamide
Breast	7	-	-	6	1	FEC-D 6 cycles (+ /- trastuzumab)	epirubicin, cyclophosphamide
Colorectal	1	3	-	-	4	mod Folfox6 12 cycles	oxaliplatin
Testicular	-	1	-	-	1	BEP 5 4 cycles	etoposide, cisplatin
Total	16	4	2	12	6		

The population of 20 patients taking antioxidant supplements with chemotherapy agents that induce oxidative stress encompassed all 14 patients who additionally ingested biologically-active herbal CAM (Table 4.4) in combinations for which it is difficult to predict potential chemotherapy interactions.[13] Two of these patients undergoing platinum chemotherapy ingested fish oil supplements, which has induced

platinum chemo-resistance in mice[243] and two additionally ingested potentially toxic apricot kernels.[245]

Table 4.4 Details of the study patients found at risk of chemotherapy interaction through antioxidant and other biologically-active CAM ingestion, with their routine CAM use prior to cancer diagnosis

Sex	Malignancy	Stage	Biologically-active CAM ingestion at chemotherapy commencement		Routine CAM use prior to cancer diagnosis
f	breast	l	vitamin A vitamin C vitamin E	vitamin B complex melatonin	homeopathy, chiropractor, bowen therapy, acupuncture regular vitamin/herbal supplements
f	breast	l	vitamin C vitamin E betacarotene resveratrol	flaxseed hemp oil glutamine probiotic	naturopaths regular vitamin/herbal supplements
f	breast	ll	vitamin C selenium sheep sorrel herb robert	milk thistle astragalus cat's claw burdock	naturopaths regular vitamin/herbal supplements
f	breast	ll	vitamin C vitamin E bue-green algae milk thistle horny goat weed ashwagandha goldthread turmeric	hawthorn grape seed boswellia flaxseed ginseng, panax quercetin bacopa hu zhang	regular vitamin/herbal supplements (purchased through internet multilayer marketing scheme)
f	breast	ll	vitamin C vitamin E CoQ10 beta-sitosterol astragalus grape seed hu zhang	turmeric coriolus mushroom maitake mushroom vitamin D folinic acid perilla	chiropractor, naturopath, acupuncture, iridology regular vitamin/herbal supplements
f	breast	ll	CoQ10 lycopene turmeric	hu zhang ginseng, panax quercetin	naturopath regular vitamin/herbal supplements
f	breast	ll	vitamin A vitamin C	papain green tea	chiropractor, acupuncture, naturopath

			vitamin E betacarotene betaine	liquorice fish oil	regular vitamin/herbal supplements
f	breast	ll	vitamin C rosehips		acupuncture chiropractor regular vitamin/herbal supplements (from friend through internet multilayer marketing scheme)
f	breast	ll	vitamin C CoQ10 barley grass	fish oil probiotic	regular self administered herbs/teas, and special diets
f	breast	ll	vitamin C CoQ10 chlorella bue-green algae turmeric	vitamin D calcium zinc magnesium probiotic	naturopath regular vitamin/herbal supplements
f	breast	ll	vitamin C vitamin E fish oil	potassium vitamin D	chiropractors acupuncture regular vitamin supplements
f	breast	ll	vitamin C reishi mushroom turmeric	green tea apricot kernels	homeopath chiropractor
f	breast	ll	vitamin C vitamin E coriolus mushroom shiitake mushroom reishi mushroom cordyceps mushroom bupleurum ginseng, panax	zizyphus pinellia ginger green tea liquorice andrographis white soapwort picrorhiza lycopene turmeric scullcap	osteopath, naturopath, acupuncture, homeopathy regular herbal supplements
f	breast	ll	vitamin A vitamin C vitamin E reishi mushroom shiitake mushroom coriolus mushroom bromelain	green tea papain diosmin rutin quercetin chlorophyll aloe vera turmeric	reiki, acupuncture, naturopath rebirthing practitioner regular vitamin/herbal supplements

f	breast	lll	vitamin C		regular vitamin supplements
m	colorectal	lll	vitamin C vitamin E betacarotene CoQ10	apricot kernels celery green tea fish oil	bowen therapy, reflexology, chiropractor bach flower
m	colorectal	lll	vitamin C betacarotene CoQ10	lycopene pau d'arco astaxanthin	naturopath regular vitamin/herbal supplements
f	colorectal	lll	vitamin C bue-green algae		homeopathy naturopath regular vitamin supplements
m	colorectal	lll	vitamin C betacarotene CoQ10		chiropractor acupuncture
m	testicular	III	vitamin C selenium "many" herbs (undeclared)	vitamin B complex vitamin D magnesium fish oil	regular vitamin/herbal supplements

4.3.3 Motivation for CAM use

CAM was used for supportive care reasons by 51% (38/75) of patients at commencement of chemotherapy treatment, the most popular being to try to improve the immune system (Figure 4.2). Other supportive care motivations were to reduce stress, lessen chemotherapy side effects, improve chemotherapy effectiveness, feel in control, boost energy, and help sleep. CAM was used by 21% (16/75) of patients to treat existing conditions unrelated to their cancer of which fish or krill oil (13/16) was the most popular. Many patients altered their diet (41%) with the aim of living a healthier lifestyle and to ensure their cancer did not return after treatment. Dietary modulation to eat more healthily was adopted by study participants through dietary advice from their CAM adviser/s, through self-motivation, or both.

Cancer treatment was the reason for CAM use by 28% of study patients (21/75); 13 patients used vitamin C, 4 patients took medicinal mushrooms and 2 patients took apricot kernels. 7 patients tried to treat their cancer by drinking lemon, sodium bicarbonate and/or proprietary "alkaline" water to try to change systemic pH or by taking diluted sodium chlorite labelled "liquid oxygen". Some patients altered their diet with the intention to treat or slow their cancer, with 13 patients stopping sugar

due to a belief that the removal of dietary sugar would "starve" cancer cells selectively and arrest cancer progression.

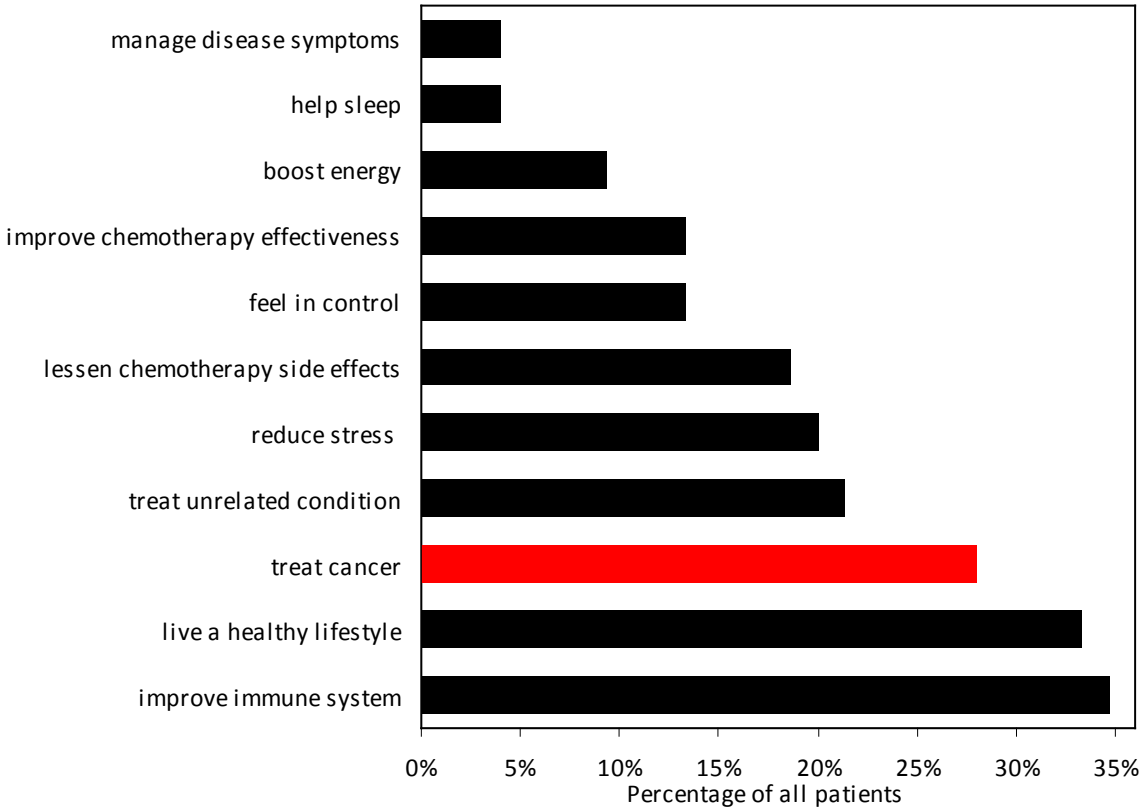

Figure 4.2 Reasons given by study patients for their CAM use at the time of commencing chemotherapy treatment

4.3.4 CAM decision-making

Patients' CAM decision-making was influenced by advice from family and friends, practitioners (CAM and conventional) either formally or informally, and from casual acquaintances met in person or on the Internet. Of the patients who engaged in CAM use, most were advised by friends (19/45) and/or CAM practitioners (19/45) of which most (13/19) were naturopaths. Other patients were self-motivated (15/45); had received CAM advice from a general practitioner (7/45); were influenced by partners (7/45), the internet (6/45), books/magazines (5/45), cancer support groups (2/45) and 3 patients received CAM advice from strangers; 2 randomly met in person and 1 on the internet.

Ten (13%) of the patients were advised not to have chemotherapy treatment (Table 4.5). In some cases this advice was given by CAM practitioners (naturopaths,

chiropractors, aromatherapist), and other patients received this advice from a friend who relayed CAM advice from her naturopath, a de facto partner, a breast cancer friend who had surgery but rejected chemotherapy, a Facebook friend never met in person, and another by a friend who was self-treating his own prostate cancer (Table 4.5).

Table 4.5 The study patients who received advice not to have chemotherapy, showing their previous CAM use, treatment completion and CAM advice-giver

Age	Sex	Malignancy	Stage	CAM advice-giver against chemotherapy treatment	Routine CAM use prior to cancer diagnosis	Completed all cycles of chemotherapy
47	f	breast	I	friend	yes	yes
47	f	breast	I	naturopath	yes	yes
62	f	breast	I	naturopath	yes	yes
39	f	breast	II	facebook friend	no	yes
45	f	breast	II	friend	yes	yes
56	f	breast	II	aromatherapist	yes	yes
65	f	breast	II	chiropractor	yes	no
70	f	breast	II	naturopath and chiropractor	yes	no
49	m	testicular	II	friend	no	yes
67	m	testicular	III	partner (defacto)	yes	yes

4.3.5 CAM use declaration

Of those patients taking oral CAM, 63% (26/41) declared their CAM use to a conventional health care provider relevant to their cancer care prior to study interview; 17 patients did so because they were asked, 6 didn't want their CAM to interfere with chemotherapy, 1 patient to "make sure CAM would assist chemotherapy", 1 patient because she wanted to know which other CAM could be recommended, and another patient because the cancer care patient booklet given in the nurse clinic recommended to do so. Reasons for patients not declaring their oral CAM use was because about half (7/15) thought it harmless, one-third (5/15) because they were not asked, 2 because of perceived rejection and lack of interest by conventional health providers and 1 patient because he had been told not to as the CAM was banned in Australia.

4.3.6 Previous CAM use

CAM was used routinely prior to cancer diagnosis by 61% (46/75) of patients, ranging from self-selected oral CAM, to regular visits to CAM practitioners such as chiropractors (13/75) and/or naturopaths (10/75) for CAM treatment and advice. Motivation for regular previous CAM use was to treat prior medical problems or for perceived maintenance of good health. The remaining 39% of study patients had never or only rarely used CAM or consulted a CAM practitioner previously. Routine prior use of CAM significantly predicted the use of potentially harmful biologically-active CAM with chemotherapy (β= +3.13, P = 0.003). The total number of 20 patients who ingested CAM of concern with chemotherapy during the study had routinely used CAM before cancer diagnosis and treatment. Conversely, none of the patients (0/29) who never or only rarely used CAM prior to cancer diagnosis were using CAM that was assessed as having the potential to modify chemotherapy effectiveness. Routine prior use of CAM predicted the use of potentially harmful biologically-active CAM with chemotherapy (β= +3.13, P = 0.003).

4.3.7 Patient CAM educational requirements

The majority of study patients (84%) would have liked to receive specific information on which CAM is safe to use with chemotherapy, before treatment commencement. Most (55/63) preferred this information as a referenced guide, 7 of these patients wanted additional verbal advice and another 7 patients identified they would prefer sole verbal advice. Patients wished to receive CAM safety information with chemotherapy at their initial oncologist consultation (46/55), either directly from their oncologist during the consultation (16/46), or either from their oncologist or other cancer care health professional (30/46) at that time.

4.4 Discussion

This is the first study the authors are aware of to examine CAM use exclusively in the adjuvant curative-intent patient population at the time of commencing chemotherapy treatment and to find that the routine use of CAM previous to cancer diagnosis is a predictor of the use of adjuvant CAM with potential to interact with chemotherapy. Study methods were aligned as much as possible to literature recommendations for CAM study survey quality[230] and the study patients' CAM ingestion was recorded by a recognised expert (pharmacist) using validated processes.[249,250]

Limitations of this study were the small sample size and that it was conducted at a single regional site, the Sunshine Coast Cancer Care Centre, so the validity of results may not necessarily be reflective of cancer patients from other day cancer centres. In 2012–13, fully immunised children aged 5 years living in the Sunshine Coast area was 88% compared to the national average of 91.5%, and the Sunshine Coast recorded the highest percentage of conscientious objection to vaccination in Australia for children aged 5 years, at 7.1%.[237] This may have implications for this study's findings, as a negative association has been found between vaccination rates with patient care by CAM providers.[251] Also, the study included a high proportion of female patients (71%) who are more likely than men to use CAM.[239] Further external multiple site studies encompassing a broader population are required to substantiate the results.

The prevalence of CAM use found in this study of 75 solid tumour cancer patients commencing curative-intent chemotherapy was 60%. This is similar to the prevalence of CAM use in a general cancer patient population (65%) previously measured in a 2010 Australian study.[6] 27% of patients in this study were taking biologically-active CAM which may have compromised their chemotherapy treatment, a similar proportion to that found in a 2004 North American study on a mixed population of 76 curative and non-curative adult cancer patients which identified 28% of patients at risk.[97] A 2013 study of patients with ovarian cancer estimated 40% were at risk of an interaction between the CAM they were taking and their prescribed chemotherapy.[116] This higher rate may be due to all patients being female and to the inclusion of patients with progressive disease who have different motivation for CAM use compared to the curative-intent study population, such as taking CAM to improve quality of life and taking more CAM risks to try to increase chances of survival.[69]

Prior CAM use has been significantly linked to CAM use with conventional cancer treatment[39] and our study replicated theses results. Indeed, all 20 patients found at risk of compromising chemotherapy effectiveness through CAM use in this study had routinely used CAM before cancer diagnosis and treatment and none of the patients who reported little or no previous CAM did so. These results were found to be significant, which suggests there is an association between previous CAM use and the use of CAM of concern with chemotherapy. This result may help cancer health

professionals better anticipate and preference CAM educational resources to previous routine CAM users.

Motivation for CAM use by study participants was predominantly for supportive care reasons. Mind-body CAM, mostly massage, meditation and acupuncture, was used by half of the study patients using CAM for supportive care treatment, showing that a significant proportion of patients seeking CAM are receptive to mind-body chemotherapy support. Although mind-body CAM evidence has been questioned due to the difficulty of producing, and often the lack of, placebo controls,[175] there is demonstrated benefit over standard care,[74,246] and when applied by appropriately trained therapists using reasonable patient-specific precautions, is safe to integrate with chemotherapy.[17] Mind-body CAM may therefore be an alternative option to effectively guide patients away from potentially harmful interactions from biologically-active CAM.

CAM was being used to treat cancer by 28% of study participants. This result, in a curative-intent population study sample, may reflect that some patients have an unrealistic expectation from CAM use and/or are not confident that their conventional treatment will be effective. The most popular CAM for cancer treatment was oral vitamin C supplementation which does not have efficacy [252] and may compromise chemotherapy effectiveness.[115] Apricot kernels, taken by two patients, are also without efficacy to treat cancer and potentially toxic.[245] CAM used by patients for pseudoscientific reasons to treat cancer such as drinking squeezed lemons in water or taking sodium bicarbonate to treat cancer by attempting to change systemic pH, drinking liquid oxygen (sodium chlorite in water), or stopping sugar with the aim of selectively "starving" cancer cells may not be harmful in their own right; however, using exclusively to delay or forgo chemotherapy in the curative setting is the greatest danger to patients.

Prior to commencing their chemotherapy treatment, 13% of study patients had received alternative health advice against having chemotherapy and to use CAM exclusively to treat their cancer. A stage ll testicular seminoma patient was advised by a prostate cancer friend to reject chemotherapy and instead use a pseudoscientific cancer "cure" product (sodium chlorite in water) found on the internet. Early stage

seminoma is a highly curable disease with conventional treatment. Fortunately this patient did not follow his friend's misguided advice and received the curative chemotherapy treatment. This occurrence exemplifies how cancer type and stage difference may be misunderstood or discounted by cancer patients and people influencing them, and that curative-intent patients may be contending with alternative treatment advice that counters evidence-based information on cancer treatment and outcome expectation.

The majority of patients taking oral CAM declared their use to a conventional health care provider when asked. Only 15% were motivated to volunteer oral CAM use because they were unsure whether it would interfere with their chemotherapy. This result is comparable to previous work that has shown cancer patients do not necessarily volunteer CAM consumption unless asked,[11] and that cancer patients prefer their health care providers to initiate discussions regarding CAM use.[15]

84% of all study participants, including some that were not taking CAM, indicated they would have liked to receive specific information on which CAM is safe to use with chemotherapy before treatment commencement, and most preferred this information as a referenced guide. A recent US survey revealed that many oncologists do not initiate CAM discussions, even with their curative-intent patients, due to their perception of having inadequate CAM knowledge.[247] Previous work indicates cancer patients would discontinue their CAM use or ask their consultant for advice if a detrimental chemotherapy interaction was suspected[97] and patients receiving chemotherapy in a day unit readily stopped CAM that was identified to be problematic on the advice of their cancer pharmacist.[253] Our study has shown that curative-intent patients (particularly those with a history of CAM use) may be taking CAM at risk of chemotherapy interaction and need to be educated that taking antioxidant supplements and/or herbal combinations with chemotherapy may compromise the effectiveness of their treatment. Patient focussed CAM-chemotherapy safety information resources may be an effective way for oncologists to explore CAM use with patients and disseminate this information.[254]

Chapter 5

Patient brochure development

5 Patient brochure development

Cancer patients require clear direction on CAM use integration to avoid biologically-active CAM potentially interfering with the effectiveness of their chemotherapy treatment. The curative-intent cancer patient study cohort (Chapter 4) reported that they would have liked to receive specific CAM-chemotherapy information, preferably in a written handout form, before commencement of chemotherapy treatment. In an attempt to provide this information to all cancer patients receiving chemotherapy, including those with progressive disease, an evidence-based educational brochure was developed.

5.1 Defining the content

In order to make it an effective educational tool the brochure's content required information acceptable to conventional cancer care professionals (especially prescribers of chemotherapy) for use in consultations, as well as information acceptable to patients.[255] The brochure was formulated following guidelines for developing patient education handouts developed in the US by Tom Lang Communications and from the Health Literacy Checklist for Written Consumer Resources, developed by Melbourne Primary Care Network in Australia.[255,256] These guidelines recommend that patient educational handouts be attractive to patients, not offend, be logically organised, visually appealing, use personal pronouns, contain awareness information rather than just facts, explain principles on why something works (or doesn't), contain strong topic sentences, use illustrations, include simple tables and lists and provide additional readings on the topic.[255] To reliably match patient educational tools with individuals, it is recommended that measuring the understanding of the actual target population is more acceptable than relying on readability formulas.[257] Therefore, the brochure was developed, using recommended guidelines, with the intent to assess readability and acceptance through surveying a representative sample of cancer patients receiving chemotherapy, using an established consumer feedback form (Appendix I).

The brochure was required to be brief, in order to not overwhelm patients already burdened by handout information, and to be as neutral as possible (neither supportive of, or against CAM use) to avoid alienating potential CAM users who may be receiving alternative CAM advice.[258] It was decided to provide patients with

evidence-based guidance on CAM safety with chemotherapy, focussing on promoting patients' CAM disclosure rather than arguing the limitations of biological CAM efficacy. A statement was included advising that no CAM has efficacy to treat cancer and that delaying conventional treatment by using CAM first may compromise cancer outcome. In this way, a neutral, unbiased tone was imparted while retaining information with an evidence base.

Mind-body CAM such as acupuncture, massage and meditation have efficacy, at least above standard care, to support patients during their chemotherapy treatment. As mind-body therapies are able to be integrated with chemotherapy safely using appropriate patient specific precautions,[17] they were recommended to patients in the brochure with the proviso that some (acupuncture, hypnosis and massage) need to be administered by trained practitioners. In keeping with neutrality, other mind-body therapies safe to use with chemotherapy, but without an evidence base, were stated in the brochure as safe to use, but were not specifically recommended. The same approach was taken for ingested CAM without biological activity, such as homeopathy. It was important to mention CAM without compelling evidence, but considered safe to use with chemotherapy, as the positive response achieved through the placebo effect when treating conditions such as pain and depressive conditions, from which cancer patients commonly suffer, can be up to 50%.[176] The rate of depression in cancer patients is three to five times higher than the general population and depression has been associated with increased mortality in breast cancer patients.[259]

The only two biologically-active CAM products recommended in the final brochure publication were ginger, which has placebo-controlled trial evidence for chemotherapy supportive care to prevent nausea,[156] and probiotics, which improved chemotherapy-induced diarrhoea in a randomised study of colorectal cancer patients.[201] The probiotic recommendation included a warning for use, as there have been case studies of patients (severely immunocompromised) developing serious probiotic infections.[202,260] Originally, fish oil was included as a recommendation due to its positive effect on countering cachexia in a lung cancer study,[204] but was removed from the final brochure publication because of a study recommending avoidance of fish oil during chemotherapy due to its potential chemo-resistance

effect.[243] In keeping with the evidence base, other biologically-active CAM were discussed in a "potential interactions" table, to explain to patients why these products may interact with chemotherapy and also to explain why they should not be used during chemotherapy treatment, or at least be considered with caution. To capture patients who are going to take biologically-active CAM anyway, for example in the circumstance when conventional chemotherapy options offer little benefit, the brochure explains how patients should provide conventional providers with information on what CAM they are taking, to enable best care for them.

The consumption of antioxidant supplements by cancer patients during chemotherapy treatment is popular but potentially problematic. The brochure discusses antioxidant supplementation with chemotherapy, identifies it as a potential problem and provides explanations as to why it may diminish chemotherapy effectiveness. It also points out that antioxidant-containing foods ingested in a normal diet are safe with chemotherapy.

The brochure's brief was to be short and concise and to put doubt into patients' minds regarding the safety of biologically-active CAM, but not to address specific CAM products. For patients requiring extra, more specific explanations on particular CAM products, the brochure included evidence-based CAM information internet resources, such as the Memorial Sloan Kettering Cancer Center and the National Cancer Institute, to guide them to safe, evidence-based sites.

The layout of the brochure was intended to maximise the inclusion of information in easy to read tabular form, with the intention of providing CAM recommendations and precautions in an easily accessed format. An evaluation study was performed before the brochure went to print (Chapter 6), and minor alterations were made to accommodate doctor and patient feedback.

5.2 Publication process

After the brochure evaluation study, the brochure information transferred neatly into an eight page, A5 booklet. The Sunshine Coast Hospital and Health Service (SCHHS) publishing unit added typeset and design features in neutral and calming colour schemes, with author consultation (Appendix H). Before the publishing

process began, required approvals were gained through completion of relevant documentation including a publication request approved by the Clinical Director of Cancer Care and the Medical Service Director at the Sunshine Coast Hospital and Health Service, Queensland, Australia. In September 2014, 300 copies of the brochure were printed for use at the Sunshine Coast Cancer Care Service (Nambour Hospital, Queensland, Australia). Due to its popularity, both with health professional staff and patients in the unit and other interested parties (for example, private clinicians, academics and community cancer care organisations), a further 800 have been printed to date.

The brochure is now available as an online resource on the Queensland Health intranet. Other health and hospital services have shown interest in using the brochure in their cancer centres. It is possible for these districts to liaise with the SCHHS for permission to print the brochure with their own health service logo added to the front cover.

Chapter 6
Evaluation of a patient CAM-with-chemotherapy educational brochure

The content of this chapter has been published as:

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6 Evaluation of a patient CAM-with-chemotherapy educational brochure

Abstract

Biologically-active CAM may detrimentally interfere with chemotherapy treatment, so cancer patients require targeted, evidence-based information on chemotherapy-CAM integration consequences. The object of this study was to investigate the potential for medical doctor recommendation and patient acceptance of a purpose designed patient educational brochure on the safe use of CAM with chemotherapy. Cancer care doctors (n=17) were provided a draft version of a patient educational brochure developed by the authors and completed a structured feedback form. Cancer patients receiving treatment (n=12) were provided with the brochure and completed the local health service consumer testing feedback form. All 17 doctors perceived a need for the brochure and all would recommend the brochure to their patients. Approximately 59% of doctors indicated they would recommend the brochure to all patients receiving chemotherapy and 41% preferred that only patients using CAM or who enquired about CAM be given the brochure. Cancer patients receiving chemotherapy reported the brochure information answered their questions and was easy to understand. This evidence-based CAM-chemotherapy patient brochure may be a useful adjunct for use by cancer care health professionals to educate patients on the potential dangers of biologically active CAM use with chemotherapy and to provide patients with safe CAM alternatives.

6.1 Introduction

The majority of patients receiving chemotherapy will consider taking complementary and alternative medicine (CAM)[6] at some time during their treatment. CAM is defined as a broad and diverse group of treatments and products that do not tend to be widely used by conventional healthcare professions.[78] Biologically-active CAM have the potential to interact with conventional medicines, including anti-neoplastic treatments[11] and herbal CAM interactions with chemotherapy have been estimated to be responsible for a substantial number of unexpected toxicities and possible under treatment of some cancers.[12] Studies on patients receiving chemotherapy have concluded that one-quarter of patients taking biologically-active herbal and/or vitamin supplemental CAM are at risk of a clinically relevant interaction.[97,261]

Mind-body CAM has shown efficacy in supportive care for patients receiving chemotherapy and when applied by appropriately trained therapists, using reasonable patient specific precautions, is safe to use at that time.[17] Mind-body therapy CAM is a safe option for cancer patients who wish to use CAM during chemotherapy.

Patients would like to receive specific information on which CAM is safe to use with chemotherapy before their treatment commences.[261] The purpose of this study was to evaluate the acceptance by doctors and consumers of an evidence-based brochure designed to provide answers to common questions chemotherapy patients have about CAM use with chemotherapy.

6.2 Methods

An educational brochure was developed by the authors (Appendix G) with the aim of providing a tool for use by cancer care doctors and associated cancer health professionals to give evidence-based guidance to patients on CAM use with chemotherapy. Eighteen doctors at the Sunshine Coast Cancer Care Service (Nambour Hospital, Queensland, Australia) were asked to provide feedback concerning the draft patient brochure through completing a structured feedback form. One doctor did not return the feedback form. Six oncologists, two oncology training registrars, five haematologists, two haematology training registrars and two general rotational hospital registrars gave written feedback. Following doctor feedback, the draft brochure was submitted to the local health service publishing unit for

publication. The relevance, clarity, presentation, readability and acceptance of the brochure were tested through distribution to 12 chemotherapy patients (Table 6.1) who each completed the Sunshine Coast Hospital and Health Service consumer testing feedback form.

Table 6.1 Demographic characteristics of the chemotherapy patients surveyed (n=12).

Characteristics	*n*
Age, years	
31-40	1
41-50	4
51-60	2
61-70	5
Sex	
F	7
M	5
Highest level of education	
Left school before year 10	1
Secondary (year 10)	4
Secondary (year 12)	3
Tertiary	4

6.3 Results

6.3.1. Doctor feedback

All 17 doctors thought there was a need for the brochure and responded that they would recommend the brochure to their patients (Table 6.2). Approximately 59% of doctors said they would recommend the brochure to all patients receiving chemotherapy but 41% preferred that only patients using CAM or asking about CAM be given the brochure. Two doctors preferred to personally give the educational CAM brochure to the patient, seven at nurse education clinic, three by the doctor or at nurse clinic and five by doctor, nurse clinic or other cancer care health professional. No doctors sought to limit the brochure to early stage/ curative intent patients.

Table 6.2 Doctor feedback with breakdown in terms of medical specialty.

	Oncologist n= 6		Haematologist n= 5		Oncology Registrar n= 2		Haematology Registrar n= 2		Rotational Registrar n= 2		Total n= 17	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Do you think there is a need for this brochure?	6	-	5	-	2	-	2	-	2	-	17	-
Would you recommend this brochure to your patients?	6	-	5	-	2	-	2	-	2	-	17	-
Which patients receiving chemotherapy would you recommend this brochure to? (more than one answer if required)												
All patients	4		3		1		2		1		10	
Patients /carers who ask about CAM or using CAM	3		2		1		0		1		7	
Only early stage/curative intent patients	-		-		-		-		-		-	
Other (specify)	-		-		-		-		-		-	
Who should give this brochure to the patient? (more than one answer if required)												
Treating consultant/ registrar	4		2		2		0		1		9	
Nurse clinic	4		5		2		2		2		14	
Other cancer care professional (specify)	1 (pharmacist)		1 (any)		1 (pharmacist)		0		1 (any)		4	
General practitioner	0		0		0		0		1		1	
Other (specify)	1 (any health practitioner that finds out patient using CAM)		0		0		1 (with other handouts in patient pack)		0		2	

Feedback received from doctors on the brochure wording and/or phrasing, when thought appropriate by the authors, was incorporated into the brochure. A haematologist indicated that it *"May be worth noting that "invasive" mind-body techniques (eg acupuncture) could be an issue in [a] setting of low platelets etc"* but did note the limitation for such details within the brochure's scope and intended broad message. Another clinician was concerned "*some fish oils have antiplatelet effect and could be an issue with haematology patients with low platelets"*. A fish oil caution was not included in the brochure because at risk patients are closely monitored, the antiplatelet effect is not great (10 g of fish oil per day has less effect on platelet function than 100 mg of aspirin given intravenously[262]) and dietary fish oil

may be consumed in amounts similar to standard supplements. One doctor sought inclusion of B group vitamins and vitamin E for the treatment of peripheral neuropathy; however, a 2008 Cochrane review concluded insufficient evidence for the use of vitamin B,[263] and vitamin E may have chemotherapy interaction complications.[114] Another prescriber's suggestion of adding grapefruit prohibition was not considered within the brochure brief.

Doctors were generally positive when optional extra feedback was given: Some comments are presented here:

> *"I think it is just right- short and balanced"*
>
> *"Overall, great idea and good brochure"*
>
> *"Good amount of writing. Messages are clear"*
>
> *"Well put together brochure. Definitely useful"*
>
> *"Excellent idea. I liked it. So many patients ask questions which this brochure is going to answer."*
>
> *"Definitely a topic poorly understood by many patients and doctors/ health care professionals. Patients often ask about the benefits/risks associated with CAMs during chemo. This brochure will help."*

One doctor criticized the brochure for being too academic; "*Needs editing for English-it's written in academic English, needs to be properly edited for patient reading"*. However the brochure was considered to be appropriate by the authors and so few changes were made; the brochure was instead submitted for publication and subsequent consumer testing to determine if it was understandable.

6.3.2 Patient feedback

Patients were generally enthusiastic about the brochure and all 12 found the information clear and easy to understand. All patients thought the information was relevant to them and that the brochure contained enough information to answer their CAM questions (Table 6.3).

> *"It's a great little book- a good size that you would read because it is not over- involved. It's matter-of-fact and gives you what you need to know in an easily understandable read. I think I would've found this booklet very beneficial when I started my regime."*

"To all concerned with the research of the publication of this information- well done"

"I found it a great and informative book: clear and to the point, thank you"

Additional patient feedback indicated that the main messages in the brochure, that biologically active CAM may interact with chemotherapy and should be declared to conventional health professionals, were understood:

"I would certainly ask more questions of the nursing staff/GP/specialist "

"Just check with your specialist first to make sure it's not going to have adverse reaction with the chemo"

"Talk to your doctor, ask questions about CAM, tell your doctor if you are taking any CAM"

"I was unaware that using "natural" remedies antioxidant, herbs could be counter productive."

The brochure was also effective in making patients aware that CAM therapies are effective and safe to use for support during chemotherapy treatment:

"Complementary therapies can work"

"Good to know about the yoga and other things which won't affect the chemo but could be substantially helpful with your wellbeing"

"Would certainly look into more of the massage, reflexology etc, also the meditation and yoga"

Table 6.3 Patient feedback, with breakdown in terms of gender and patient malignancy (Haem = Haematology; Oncol = Oncology), and numbers indicating those who answered yes (Y), no (N) or did not answer the question (na).

	Total n=12		Female n=7		Male n=5		Haem n=4		Oncol n=8	
	Y	N/na	Y	N/na	Y	N/na	Y	N/na	Y	N/na
Did you find the information clear, easy to read and understand?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Was there enough information to answer your questions?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Did the information explain medical terms well?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Do you believe this information is relevant to you?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Is the content culturally sensitive and appropriate?	10	0/2	5	0/2	5	0	3	0/1	7	0/1
Is the design appropriate and appealing?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Is the design clear, uncluttered, and easy to follow?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Is the print large and clear enough?	12	0/0	7	0/0	5	0	4	0/0	8	0/0
Did the photos and illustrations help you understand the information?	11	0/0	6	1/0	5	0	3	1/0	8	0/0

6.4 Discussion

The evidence-based educational brochure was designed to be brief and as neutral as possible; neither supportive of, or against CAM use. The authors deemed this necessary to not alienate potential CAM users who may be receiving alternative CAM advice.[17] Chemotherapy patients are likely to be contending with CAM advice from a variety of sources including family, friends, practitioners and even casual acquaintances, who may be particularly insistent and persuasive when they regard themselves as having CAM expertise.[6,10,16,261] Conventional health practitioners need to provide evidence based CAM information to chemotherapy patients to counter CAM misconceptions patients may have and to guide patients away from taking CAM which may be potentially detrimental to their treatment.

All cancer care doctors indicated they would use the brochure for their patients. A proportion of doctors wanted only patients asking about or using CAM to receive the brochure. These doctors were concerned that giving CAM information to patients may be misconstrued as being promotional of CAM use with chemotherapy and one patient did report she would look into more mind-body CAM and supplements that may help if she were able to take them, as a result of reading the brochure. If only patients who ask about CAM were offered the brochure, patients in need of CAM guidance with chemotherapy may be missed; cancer patients do not necessarily volunteer their CAM consumption unless asked,[11] prefer their health care providers to initiate discussions regarding CAM use,[15] want safety information regarding CAM with chemotherapy before they start treatment,[261] and make CAM decisions at the same time as standard medical decisions.[10]

Though there are existing general information resources on CAM use, chemotherapy patients want to receive specific evidence-based information on CAM use at the time of receiving chemotherapy.[261] This small population study demonstrated that a brochure showed promise in providing cancer patients' educational requirements on the safe use of CAM with chemotherapy and may be a useful tool for use by cancer care health professionals to educate patients on potential dangers of biologically active CAM use with chemotherapy and to provide patients with safe CAM alternatives if required.

Chapter 7

The use of a brochure to enable CAM-with-chemotherapy patient education

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7 The use of a brochure to enable CAM-with-chemotherapy patient education

Abstract

The majority of cancer patients receiving chemotherapy will consider taking complementary and alternative medicine (CAM) during their treatment. As biologically-active CAM may detrimentally interfere with chemotherapy treatment, cancer patients require evidence-based information on chemotherapy-CAM integration consequences. This study aimed to assess if the availability of a purpose-designed brochure within a cancer service aided doctors' discussions with their patients on CAM use and helped patients understand the effects of CAM during their chemotherapy treatment. Cancer care doctors consulting in an adult day unit completed a structured post-intervention feedback survey form (n=17), and cancer patients receiving chemotherapy treatment were provided the brochure and completed the local health service consumer testing feedback form (n=30). All cancer care doctors perceived a need for the brochure, and recommended the brochure to their patients. All doctors thought the brochure made it easier for them to discuss CAM with their patients and 59% believed that it saved them time during patient consultations. 90% of cancer patients reported the brochure had enough information to answer their CAM questions and all patients thought the information was easy to read and understand. An evidence-based CAM-with-chemotherapy patient brochure was perceived to have enabled cancer care doctors to discuss CAM with their patients and to have answered patients' CAM questions.

7.1 Introduction

A recent US survey revealed that less than half of oncologists initiate complementary and alternative medicine (CAM) discussions with their patients, mainly due to a perception of having inadequate CAM knowledge.[264] CAM is defined as a broad and diverse group of treatments and products that are not widely used by conventional healthcare professions.[2] The term CAM is used for the purpose of this study; however, of note is that The National Center for Complementary and Alternative Medicine (NCCAM) has changed its name to National Centre for Complementary and Integrative Health (NCCIH) and uses the term "integrative" in preference to "alternative". The majority of patients receiving chemotherapy will consider utilizing CAM at some time during their treatment[6] and even curative-intent patients, who

require assured dose intensity for best outcomes,[240] may be using CAM with potential to compromise the effectiveness of their chemotherapy treatment.[258] As one-quarter of patients taking herbal and/or vitamin supplemental CAM are at risk of a clinically relevant interaction with their chemotherapy,[97] it is important that patients receive evidence-based information on the potential consequences of chemotherapy-CAM integration.

Cancer patients may be contending with pseudoscientific alternative treatment advice, from family, friends or CAM practitioners, that counters evidence-based information on cancer treatment and outcome expectation.[258] Cancer care health professionals should therefore openly discuss CAM with their patients and ensure evidence-based CAM information is offered to them.[265] Though there are existing general information resources for cancer patients on CAM use, targeted education addressing CAM use during active treatment is required. Over 80% of curative-intent cancer patients indicated that, before treatment commences, they would like specific information on which CAM is safe to use with chemotherapy.[258]

In an endeavour to provide CAM-chemotherapy information to cancer patients, an evidence-based educational brochure was developed based on current evidence. Information needed to be acceptable to both conventional cancer care professionals (especially prescribers of chemotherapy) and also to cancer patients, to make it an effective educational tool.[255] The brochure was also required to be brief, to not overwhelm patients already burdened by handout information, and to be as neutral as possible, neither supportive or against CAM use, to avoid alienating potential CAM users who may be receiving alternative CAM advice. To keep the brochure concise, it was decided to provide patients with evidence-based guidance on CAM safety with chemotherapy; to promote caution and CAM disclosure rather than argue the limitations of biological CAM efficacy. A statement was included to the effect that no CAM has efficacy to treat cancer and that delaying conventional treatment by using CAM first may compromise cancer outcome. In this way, a neutral, unbiased tone was imparted while retaining information with an evidence base.

Mind-body CAM therapies such as acupuncture, massage and meditation have efficacy, at least above standard care, to support patients during their chemotherapy

treatment.[17] As mind-body CAM therapies are able to be integrated with chemotherapy safely, when applied by appropriately trained therapists using reasonable patient specific precautions, they were recommended to patients in the brochure. Other mind-body CAM safe to use with chemotherapy but without an evidence base were listed in the brochure as safe to use with chemotherapy, but were not specifically recommended. The same approach was taken for ingested CAM without evidence for biological activity such as homeopathy. In this way, CAM that is without compelling evidence but is safe to use with chemotherapy was included in the brochure because patients who wish to use it may benefit from a placebo effect; the positive response achieved by placebo when treating conditions such as pain and depression, from which cancer patients commonly suffer, can be as high as 50%.[176]

The only two biologically-active CAM products included in the final brochure as recommendations were ginger, which has placebo-controlled trial evidence for chemotherapy supportive care to prevent nausea,[156] and probiotics, which improved chemotherapy-induced diarrhoea in a randomised study of colorectal cancer patients.[201] The probiotic recommendation in the brochure included a warning to not use if very ill as there are case studies of patients (severely immunocompromised) developing serious infections associated with probiotic use.[202,260] Originally, fish oil was included as a recommendation due to its positive effect on countering cachexia in a lung cancer study,[204] but was removed from the brochure because of a recent study recommending fish oil be avoided during chemotherapy due to its potential chemo-resistance effect,[243] though more research is required to support this associative study's negative finding. Other biologically-active CAM were included in a "potential interactions" table, to explain to patients why these products may interact with chemotherapy and also to explain why they should not be used or at least be considered with caution. The consumption of antioxidant supplements during chemotherapy treatment is popular but potentially problematic.[112] The brochure identifies antioxidant supplementation with chemotherapy as a potential problem and provides an explanation why it may diminish chemotherapy effectiveness. To capture patients who are going to take biologically-active CAM anyway, for example in the circumstance of conventional chemotherapy options offering little benefit, the brochure explains in a final statement that patients should provide their cancer

specialist or pharmacist with information on any CAM they are taking to ensure the best care can be provided for them.

The layout of the brochure was intended to maximise the inclusion of information in easy to read tabular form, with the intention of providing CAM recommendations and precautions in an easily accessed format. The design, content and potential, acceptance of the first edition of the brochure was assessed prior to implementation,[254] and a second edition incorporating minor changes was then published and distributed. In the present study we describe cancer doctors' acceptance and use of the brochure in an adult day cancer centre and assess whether the brochure helped cancer patients understand the effects of CAM use during their chemotherapy treatment.

7.2 Methods

A published educational brochure (Appendix H) in use at the Sunshine Coast Cancer Care Service (Nambour Hospital, Queensland, Australia) for 6 months was assessed in April 2015 by cancer care doctors who prescribe chemotherapy (oncologists, haematologists and registrars) and adult patients receiving chemotherapy in the cancer day unit. All cancer doctors were asked to provide feedback concerning their use of the patient brochure through completing a structured feedback form. Questions included whether the brochure is needed, was being recommended by them to patients, whether the brochure made it easier for them to discuss CAM with patients and whether the brochure saved them time during consultations. Doctors were also asked whether all or just certain populations of their patients receiving chemotherapy were offered the brochure. Other questions to doctors elicited their opinion on who should distribute the brochure to patients, recommended changes to the brochure and any other feedback. The relevance, clarity, presentation, readability and acceptance of the brochure were tested through distribution to consecutive day unit cancer patients receiving chemotherapy, who completed the Sunshine Coast Hospital and Health Service consumer testing feedback form. Participants were given the option of either completing the feedback form in the day unit or through returning the form by mail using a supplied prepaid envelope. The study was granted ethics exemption for publication by Human Research Ethics Committees at The Prince Charles Hospital and The University of Queensland.

7.3 Results

7.3.1 Doctor feedback

Six oncologists, 2 training oncology registrars, 6 haematologists, 3 haematology registrars (1 training and 2 general) gave written feedback. One doctor (general registrar) did not return the feedback form. All 17 cancer care doctor participants thought there was a need for the brochure, reported that they recommend the brochure to their patients, and thought the brochure made it easier to discuss CAM with their patients (Table 1). Over half (59%) reported that it saved them time during patient consultations, however 29% disagreed and two were not sure whether it saved consultation time as they had not used the brochure enough. Of those that disagreed, one oncologist commented that, *"checking specific medications or supplements requires a review of more detailed/ specific information on the product which is not in the scope of the booklet"*, and another oncologist thought the brochure took more consultation time because it *"has led to discussion which previously patients may not have raised with the medical team"*. Only 35% of doctors indicated that they recommend the brochure to all patients receiving chemotherapy, preferring to provide it to patients that they were aware were taking CAM (59%) or patients/carers who asked about CAM (70%). Almost all of the doctors (88%) believed the treating doctor should give the brochure to their patients, though most doctors (70-76%) thought a variety of sources would be appropriate to distribute the brochure to their patients, including nurses and pharmacists involved in providing care, and displaying the brochure in the clinic waiting area. The clinic education nurse received the most votes (53%) as the preferred person to distribute the brochure to patients (Table 7.1). No doctors sought to limit the brochure to early stage/ curative-intent patients. Additional written doctor feedback is listed in Supplementary Table 7.1.

Table 7.1 Doctor feedback with breakdown in terms of medical specialty and numbers indicating those who answered yes (Y), no (N) or did not answer the question (na)

	Oncologist n= 6		Haematologist n= 6		Oncology Registrar n= 2		Haematology Registrar n= 3		Total n= 17	
	Y	N	Y	N/na	Y	N	Y	N/na	Y	N/na
Do you think there is a need for this brochure?	6	-	6	-	2	-	3	-	17	0
Do you recommend this brochure to your patients?	6	-	6	-	2	-	3	-	17	0
Do you think the brochure makes it easier for you to discuss CAM with your patients?	6	-	6	-	2	-	3	-	17	0
Has the brochure saved you time during patient consultations?	5	3	4	1/1	2	-	1	1/1	10	5/2
all patients receiving chemotherapy	2		3		0		1		6	
patients you know are using CAM	3		4		2		1		10	
patients/carers who ask about CAM	5		3		2		2		12	
only early stage/curative intent patients	-		-		-		-		0	
I wouldn't recommend it to any patients	-		-		-		-		0	
other	-		1		-		-		1	
treating consultant/ registrar	6		5		2		2		15	
nurse at clinic education	5		4		2		1		12	
any nurse in cancer care day unit	5		5		1		1		12	
cancer pharmacist	5		5		2		1		13	
any health professional in cancer care day unit	2		6		1		3		12	
displayed in day unit waiting room (for anyone to take)	5		5		2		1		13	
general practitioner	1		4		1		1		7	
other (specify)	0		0		0		0		0	
treating consultant/ registrar	1		-		1		1		3	
nurse at clinic education	5		3		-		1		9	
any nurse in cancer care day unit	-		-		-		-		0	
cancer pharmacist	-		2		1		-		3	
any health professional in cancer care day unit	-		-		-		1		1	
displayed in day unit waiting room (for anyone to take)	-		1		-		-		1	
general practitioner	0		-		-		-		0	
other (specify)	0		-		-		-		0	

7.3.2 Patient feedback

40 day unit chemotherapy patients were asked to participate in the study of which 30 (demographic characteristics listed in Table 7.2) completed the Sunshine Coast Hospital and Health Service consumer testing feedback form. 7 patients did not return the form and 3 patients declined the study. All patient participants (n=30) found the information clear and easy to understand, the design appealing and the print large and clear enough. 97% of patients found the brochure easy to follow. 90% of patients thought the information was relevant to them and 90% also thought the brochure contained enough information to answer their CAM questions (Table 7.3). Additional written patient feedback is listed in Supplementary Table 7.2.

Table 7.2 Demographic characteristics of patient participants (n=30)

Characteristics	*n*
Age, years	
21-30	1
31-40	1
41-50	5
51-60	5
61-70	12
71-80	4
81-90	2
Sex	
F	17
M	13
Highest level of education	
Left school before year 10	6
Secondary (year 10)	7
Secondary (year 12)	4
Secondary + TAFE	7
Tertiary	4
Tertiary + Post grad	2

Table 7.3 Patient feedback, with breakdown in terms of gender and numbers indicating those who answered yes (Y), no (N) or did not answer the question (na)

	Total n= 30		Female n= 17		Male n= 13	
	Y	N/na	Y	N/na	Y	N
Did you find the information clear, easy to read and understand?	30	0/0	17	0/0	13	0
Was there enough information to answer your questions?	27	2/1	14	2/1	13	0
Did the information explain medical terms well?	30	0/0	17	0/0	13	0
Do you believe this information is relevant to you?	27	3/0	16	1/0	11	2
Is the design appropriate and appealing?	30	0/0	17	0/0	13	0
Is the design clear, uncluttered, and easy to follow?	29	1/0	17	0/0	13	0
Is the print large and clear enough?	30	0/0	17	0/0	13	0

7.4 Discussion

All cancer care doctors participating in this study recommend the brochure to some or all of their patients and find the brochure makes it easier to discuss CAM with their patients. Cancer patients do not necessarily volunteer their CAM consumption unless asked,[11] and prefer their health care providers to initiate discussions regarding CAM use.[15] The brochure's recommendation and distribution during the cancer care consultant clinics is timely as cancer patients make CAM decisions at the same time that they make standard medical decisions.[10] Patients may not reveal their CAM consumption if they anticipate a negative response or do not wish to risk their relationship with their oncologist[183] and patients report higher satisfaction with their clinic visit when CAM is discussed.[266] The brochure's existence and recommendation

implies an interest in patients' CAM use, which was welcomed; *"that complementary practices are understood and valued by this hospital", "it is appreciated that staff at Nambour Hospital are available to discuss these issues and patient queries and concerns*".

Most doctors recommend the brochure to patients who ask about CAM, "*Yes, informative and well-presented brochure. I would have no hesitation in giving brochure to patients who enquired about the use of CAM in cancer care*". However, discussion around CAM consumption is not always initiated by the patient[265] and a haematologist commented as such: *"If it is given out routinely (to all patients) would promote patients discussing CAM if not prepared to raise it themselves"*. To ensure no patients that are utilizing CAM, or may consider commencing CAM use, are missed, all patients should receive the brochure at the start of chemotherapy treatment. Only 35% of cancer care doctors recommended the brochure to all patients receiving chemotherapy, which indicates that some chemotherapy patients do not receive the brochure and associated explorative conversation during their initial consultation from their consultant, their preferred CAM information source, at the time they are likely to be making CAM decisions.[265] 76% of cancer care doctors identified they were happy for the brochure to be displayed in the waiting area for anyone to take, which would enable access to patients who are taking CAM but don't otherwise ask; however, further education of cancer doctors is required to encourage better anticipation and information provision to patients who are considering using CAM with chemotherapy but do not reveal their intention.

Cancer patients are likely to be influenced in their decision-making by significant others to take CAM: family, friends and even casual acquaintances met in waiting rooms and support groups.[6,10] Some patients used the brochure as a talisman to ward off well-meaning but potentially dangerous advice. One patient commented he would *"share the info with my carers and those, with the best intent, urging me to take this and that,"* another; *"friends constantly tell one that such & such is great, But…"*.

Some patients indicated that they would like to have seen more detailed information, and a haematologist gave feedback, *"?additional interaction eg velcade(bortezomib)/ green tea"*, though the interaction significance of bortezomib and green tea has been

challenged in a preclinical study.[267] The brochure's intent was to provide patients with evidence-based guidance on CAM safety and to promote caution and CAM disclosure rather than provide specific information on individual products. The brochure contains a recommendation for patients to visit internet sites with evidence-based CAM information resources such as the Memorial Sloan Kettering Cancer Center and the National Cancer Institute for further CAM information. It is important to try and guide cancer patients away from pseudoscientific internet cancer product merchandisers whose arguments may be seductive.[11] Patients should also be made wary of what they read as, for example, two-thirds of articles in Australian newspapers describe CAM cancer treatments in the context of a cure.[163] The brochure was effective in making patients cautious about using CAM *"be careful, consult with doctor before indulging in CAM", "the unproven benefits of CAM, the interactions of various CAM with my treatment regime", "there has not been enough research on medicine based CAM*".

Cancer patients feel better about themselves and their treatment when empowered to make their own decisions,[10] and the majority of patients (90%) in this study thought the brochure contained enough information to answer their questions. An oncologist commented that the brochure was able to "*promote patients on to an evidence-based path*". This small post-intervention quality assurance study found the availability of a purpose-designed CAM brochure within a cancer service aided discussions between doctors and their patients on the effects of CAM, helped patients understand the potential effects of CAM during their chemotherapy treatment and may save doctor consultation time. As the study was conducted at a single site, it has the limitation that cancer patients attending, and cancer doctors practicing, at the Sunshine Coast Cancer Care Service may not be representative of patients and cancer consultants at other sites. Further studies at different cancer centres are required to substantiate the positive reception for the educational CAM-with-chemotherapy brochure established in this study.

Supplementary Table 7.1 Additional written doctor feedback

Do you think the brochure makes it easier for you to discuss CAM with your patients?	
Oncologists	• Reminder to discuss CAM/ non-prescribed meds • Offers a starting point which actually clarifies the initial questions patients have • It is easy to read and follow. Patients often ask about alternative treatment
Oncology registrar	• clear, easy to follow
Haematologists	• If it is given out routinely (to all patients) would promote patients discussing CAM if not prepared to raise it themselves. • Provides good summary of medicine and non-medicine based CAM
Haematology registrar	• Should a patient express an interest in CAM, I would be very happy to give them this brochure [if] not prepared to raise it themselves. • I think this is important to discuss CAM with chemo patients as practically speaking, quite a few pts are inclined towards CAM & it's very important to tell them the interactions of herbal/ chinese meds with chemo meds.
Has the brochure saved you time during patient consultations?	
Oncologists	• Most of the time is consumed discussing/ checking specific medications or supplements and this requires a review of more detailed/ specific information on the product which is not in the scope of the booklet • It is easier to refer patients to the brochure if there is less time • has led to discussion which previously patients may not have raised with the medical team • Have not used it enough. Generally should help.
Haematologists	• haven't used yet but believe it will • not used it yet but I imagine it would
Haematology registrar	• patients (to date) have not mentioned CAM in my clinics • I found it very useful. I think it should be discussed with all patients receiving chemo. • Some patients may not reveal their inclination towards CAM & therefore it's important to discuss with them
Extra feedback and/or suggested additions or omissions for the next brochure edition	
Oncology registrar	• Yes, informative and well-presented brochure. I would have no hesitation in giving brochure to patients who enquired about the use of CAM in cancer care.
Haematologists	• I think this is valuable to promote patients onto an evidence based path if they are considering alternative therapy • I have given a few to my husband's (GP) clinic • I would try and publish something about it in the LMA (local medical association) newsletter • ?additional interaction eg velcade/ green tea
Haematology registrar	• I find the brochure very helpful as the majority of patients enquire about issues such as alternative medicine, life style, sports and meditation • I suggest a strong emphasis be made in the brochure that although following a healthy diet or life style is good to keep the patient in a better performance status, this is not an alternative to specific cancer directed therapy • I think it's important that all the registrars, particularly the ones doing clinic, should go through the brochure and discuss with the patient (about to start chemo) the important aspects about CAM

Supplementary Table 7.2 Additional written patient feedback

Did you find the information clear, easy to read and understand?

- I think it's a very good publication
- very well set out
- well set out, easy to understand language
- liked summaries
- references should be on same page as the reference number
- provides valuable background information
- was pretty straight forward, easy to understand
- subtopics limited to a paragraph makes reading easy and able to remain attentive to subject
- yes, well set out and easy to read

Was there enough information to answer your questions?

- wasn't overwhelming but very informative
- bit more info on vitamins, when you can and can't take them
- would it be useful mentioning other supplements such as glucosamine, lysine, other joint and arthritis supplements, sleep supplements etc if there is a possibility that they could also be harmful
- no specifics on doses of vitamins/ herbal ,mixtures etc. How much is too much?
- dispel the myths of alternative treatment. Good intentions doesn't necessarily correlate with a treatment regimen
- yes, some new info in pamphlet

What were the main messages?

- the unproven benefits of CAM. The interactions of various CAM with my treatment regime
- do not mix CAM with chemo treatment
- that mind-body therapy CAM seems very good
- that mind-body CAM is the most important when looking for complementary cancer care. That all other medication (CAM) should be checked with doctor
- that you can do other treatments on chemotherapy
- don't use alternative medicines with your chemo unless you consult your doctor first
- that complementary practices are understood and valued by this hospital
- is not worth the risk of interfering with chemotherapy effectiveness
- herbs etc might interact with chemo, not enough research
- discuss what you are taking with your doctor
- that mind-body therapy CAM was safe and helpful when having chemotherapy
- there has not been enough research on medicine based CAM, which can potentially reduce the effectiveness of chemo and cause side-effects
- safe for mind-body therapies
- risk of ineffective treatment outcome if CAM used
- refer to doctor before undertaking alternative or complementary medicines
- very helpful regarding herbal medicines, excellent
- provides clarity re CAM and relationship with conventional treatment
- to use common sense and enable decision for your well being
- what CAM is safe with chemo
- advise if you are taking any supplements
- how to care for yourself
- some things are definitely good- others not sound
- be careful, consult with doctor before indulging in CAM
- food and alternative medicines which have potential to impact on chemo
- mind/body therapy is beneficial during chemotherapy, CAM may interact in a negative way during chemo

What do you feel you should do as a result of reading this resource?

- share the info with my carers and those, with the best intent, urging me to take this and that.
- complete the chemo treatment I am on at the moment
- keep on doing what my oncologist suggested
- continue with Tai Chi daily, keep up my painting, walking, reading, social activities
- look into complementary and alternative medicine more
- consider all options, practice more mind-body therapies
- take no other products or treatments until chemotherapy is completed
- feel confident with usage of some complementary treatments
- be careful what you take with chemo
- stop using any potentially harmful CAM and check with the hospital pharmacy if any other medications I am taking could react with chemotherapy
- look at suggested websites for more information
- nothing CAM
- valuable education tool for treatment plan
- check (CAM) with chemist beforehand
- nothing I already have been doing; exercise, meditation, visualization
- be careful of what I take
- should have read this book properly a lot earlier through my treatment
- keep it handy
- nothing, I have not used any CAM
- helpful to receive this information at the time I have chemo
- avoid those foods and alternative medications that may affect chemotherapy

Are there any other comments or suggestions that you would like to make?

- perhaps a list of food groups which may complement diet whilst receiving chemotherapy
- perhaps a little more detail about physical activities (ie: yoga, walking etc)
- Thank you! Perhaps some info re super food trend, if there is an interaction
- an easy to follow guide that would be good for all patients undergoing chemotherapy
- it is appreciated that staff at Nambour Hospital are available to discuss these issues and patient queries and concerns
- unfortunately hospital treatments are focused on your surgery, chemo, radiation with a small space for dietician and psychology support. I am much more than my body, so therapies (CAM) that help with emotional and spiritual side are important too. You want to complement your treatment, not interfere with it.
- I thought you were supposed to exercise, pamphlet says mild exercise. My mild exercise might be just about nothing
- perhaps mention of time frame for when after treatment finished it would be safe to continue CAM for existing conditions or for assisting recovery
- well presented and easy to follow
- a very good idea because friends constantly tell one that such &such is great, But…
- good arrangement of information, colour scheme of brochure good and appealing
- good size -enough info without over info to make it confusing
- use of tables gives clear understanding
- can’t find fault with brochure- very good

Chapter 8

Discussion

8 Discussion

The aims of this thesis were to establish what extent adult cancer patients receiving curative-intent chemotherapy potentially compromise their treatment and/or safety by using complementary and alternative medicine (CAM) and to identify which cancer patients use CAM at this time, why they use it, and who are most at risk. Additionally, it aimed to establish whether there was a need for an educational intervention to guide cancer patients on the safe use of CAM with chemotherapy, develop and publish the educational intervention and to evaluate the effectiveness of the intervention through surveying cancer patients and cancer care professionals, particularly doctors.

The literature review of CAM use during chemotherapy treatment (Chapter 2) found that the cohort of cancer patients most at risk from taking biologically-active CAM with adjuvant chemotherapy treatment were those being treated with curative intent. The subsequent study on a consecutive sample of curative-intent cancer patients at the Sunshine Coast Cancer Care Services Day Unit, Nambour Hospital, Queensland, Australia (Chapter 4) found 60% of study patients commencing curative-intent chemotherapy were using CAM at the time of receiving chemotherapy which is a similar rate to 65% measured in a previous Australian study of cancer patients.[6] This figure is not as high as found in a 2014 Australian study on CAM use by a mixed population of cancer patients receiving radiation treatment (78% when prayer was excluded as CAM use).[268] In the present study (Chapter 4), answering research question 1, one-quarter (27%) of patients were taking biologically-active CAM that may have compromised their chemotherapy treatment. This is a similar proportion to that found in the US for a mixed population of curative and non-curative adult cancer patients that identified 28% of patients at risk.[97]

The motivation for CAM use by study participants was predominantly for supportive care reasons. Mind-body CAM, which may be used safely with adjuvant chemotherapy, was used by half of the study patients using CAM for supportive care treatment. Over a quarter of study participants were trying to treat their cancer using CAM that has no evidence for efficacy. Answering research question 2, it was found study participants' CAM decision-making was influenced by advice from family and friends, practitioners and casual acquaintances.

Resolving research question 3, the study (Chapter 4) identified a clear need for an educational intervention, finding that over three-quarters of the patient participants wanted specific safety information on CAM integration with chemotherapy, preferably as a written handout. An educational tool, designed to advise cancer patients how to navigate CAM-chemotherapy integration safely, was developed for use and distribution by cancer care professionals (Chapter 5). To answer research question 4, the educational tool was evaluated in a quality assurance study (Chapter 6), which showed potential for medical doctor and patient use and feedback from target populations was incorporated into the brochure. After implementation and use within the Sunshine Coast Cancer Care Service, Nambour Hospital, Queensland, Australia, a further quality assurance study (Chapter 7) found the brochure intervention to be effective in aiding discussions between doctors and their patients on the effects of CAM, and helped patients understand the potential effects of CAM during their chemotherapy treatment, answering research question 5. The findings for the thesis research questions and aims and objectives achieved are further discussed in the following key thesis results.

8.1 Key thesis results

In a population sample of curative-intent cancer patients, one quarter were taking biologically-active CAM that theoretically may have altered the dose intensity of their adjuvant chemotherapy treatment.

To date there is not sufficient evidence to determine whether biologically-active CAM antioxidants taken by 27% of the study population (Chapter 4) exert a positive or a negative effect with adjuvant cancer treatment.[242] However, considering the narrow therapeutic window of anticancer drugs, relatively small changes in dose intensity that may occur due to antioxidant activity have the potential to compromise treatment effectiveness. Antioxidant supplements are often used by cancer patients with the motivation to reduce chemotherapy side effects, but their efficacy to ameliorate chemotherapy side effects is yet to be determined.[242] It has been proposed that the use of antioxidant supplementation by cancer patients to reduce toxicity may be at the cost of diminishing the effectiveness of chemotherapy by protecting tumour cells

from oxidative damage.[112] A randomized, placebo-controlled trial of cancer patients taking supplemental antioxidants to reduce side effects of adjuvant radiotherapy demonstrated that these patients had worse survival outcomes after their radiation treatment. [117] As the primary mechanism of action of many chemotherapy agents is similar to radiotherapy, through the generation of reactive oxygen species (ROS), it is reasonable to equate these results. A more recent general review of the use of antioxidants with adjuvant cancer treatment concluded it was difficult to determine whether antioxidants affect treatment outcomes but cautioned that for curative regimens, it is important not to inhibit therapy in any way.[242]

One quarter of the study sample of curative-intent cancer patients (Chapter 4) took antioxidants, placing them at risk of diminishing their cancer treatment outcome through reducing their effective adjuvant chemotherapy dose intensity. 70% of these patients additionally took herbal combinations that had the potential to interact with chemotherapy (positively or negatively) but not enough is known to allow any predictions to be made.[13] Herbal CAM interactions have previously been attributed to a substantial number of unexpected toxicities and under-treatment seen in cancer patients receiving adjuvant chemotherapy.[11,12]

There is a significant association between cancer patient routine use of CAM prior to cancer diagnosis and their use of biologically-active CAM at risk of compromising chemotherapy effectiveness

Prior CAM use has been significantly linked to CAM use with conventional cancer treatment in a study of 403 mixed curative and palliative adult cancer patients treated at an ambulatory treatment unit in Singapore.[39] Though this study captured oral CAM usage, it did not specify prior CAM use or estimate the significance of the prior CAM use with chemotherapy treatment. All curative-intent patients (Chapter 4) found to be at risk of compromising their chemotherapy effectiveness through biologically-active CAM use had routinely used CAM before cancer diagnosis and treatment. This significant result suggests an association between previous CAM use and CAM use of concern with adjuvant chemotherapy. This routine CAM use prior to cancer diagnosis was self-selected oral CAM and/or involved regular visits to CAM practitioners, such as chiropractors and/or naturopaths, for CAM treatment and

advice. Motivation for regular previous CAM use was to treat prior medical problems or for perceived maintenance of good health. This finding of an association between previous CAM use and the use of CAM of concern with chemotherapy may help cancer health professionals better anticipate and preference CAM educational resources to previous routine CAM users.

Cancer patients receiving curative-intent chemotherapy treatment may be receiving advice from CAM advisers not to have chemotherapy

Thirteen percent of study participants (Chapter 4) were advised by CAM practitioners, family members, friends and strangers not to have chemotherapy treatment. This is concerning, as timely adjuvant chemotherapy treatment in the curative-intent cancer patient population correlates positively with their disease-free and overall survival.[241] These study participants were contending with alternative treatment advice to use only CAM to treat their cancer, which counters evidence-based information on cancer treatment and outcome expectation. This result, in the patient group who presented for their chemotherapy treatment despite being advised not to, points to the possible existence of unseen patients who may have delayed or even rejected chemotherapy treatment on the recommendation of CAM advisers.

CAM advisers may also demonise conventional cancer treatment, and this may have a nocebo effect.[160,161] A nocebo effect occurs when verbal suggestions of negative outcomes result in a patient expecting and actually experiencing clinical worsening of the condition.[182] It would seem logical that the group of study participants (13%) who were advised by CAM practitioners, family members, friends and strangers not to have chemotherapy treatment faced the possibility of the nocebo effect actually worsening their response to chemotherapy.

Cancer patients want to receive information on which CAM is safe to use adjuvant with chemotherapy, before treatment commencement

Most (84%) of study participants (Chapter 4) indicated they would have liked to receive specific information on which CAM is safe to use with chemotherapy before the commencement of their treatment. Most preferred to receive this information in a

referenced guide**,** from conventional cancer professionals, especially their cancer care doctor**.**

Some patients were receiving advice from CAM information providers that conflicted with conventional care. This advice extended to encouraging cancer patients to choose biologically-active CAM that may have risked both patient safety and chemotherapy treatment effectiveness. Cancer patients require evidence-based information to enable them to make informed decisions on which CAM can be used safely with adjuvant chemotherapy.

An evidence-based CAM-with-chemotherapy patient brochure may be a useful adjunct for use by cancer care health professionals to educate patients on the potential dangers of biologically-active CAM use with chemotherapy and to provide patients with safe CAM alternatives.

In the post-intervention brochure study (Chapter 7), it was shown that specific information on CAM use with chemotherapy contained in a purpose-designed, evidence-based patient brochure proved effective in being able to answer most cancer patients' CAM information needs. The brochure also provided cancer professionals with an effective CAM information tool they were happy to provide to their patients.

This brochure enables a united, evidence-based voice on CAM information dissemination from all health professionals working in cancer care. It has been observed where patient and medical perspectives diverge, cancer care nurses have aligned with patients and have also given contradictory advice.[269] Use of such a brochure in the cancer care setting may avoid the possibility of health professionals reinforcing non evidence-based CAM advice and potentially adding to patients' confusion and anxiety about what to do about CAM integration.

Any contradictions in their CAM advice may cause cancer patients considerable anxiety, particularly when they are making conventional treatment decisions, as their disease is often treated quickly, with little time for consideration and debate. In this context the brochure can be used to show patients that conventional cancer care

professionals know about CAM and can guide cancer patients on how to integrate CAM safely with their chemotherapy if they wish to do so.

The brochure has brought consistency to the evidence-based message patients receive from cancer care professionals at the Sunshine Coast Cancer Care Service. Additionally, cancer care professionals who were not surveyed in the thesis studies have welcomed the educational tool. Cancer pharmacists use it in conjunction with the taking of patients' medication histories and nursing staff and allied health professionals, including psychologists, dieticians and social workers, use it in their practice at the cancer care service unit. The brochure is also used outside its original domain. Copies have been taken from the Sunshine Coast Cancer Care Service and displayed in private cancer clinic waiting rooms on the Sunshine Coast and in Brisbane, it is used in community cancer care organisations on the Sunshine Coast, and university academics have used the brochure for teaching purposes.

Other Queensland government health service district cancer care centres have shown interest in using the brochure. A further post-evaluation study involving these centres, as well as other interstate and international cancer service centres, would be useful to gauge whether the brochure translates to cancer centres which may have a different patient and health professional demographic. The brochure may also translate for use by general practitioners and other community-based health professionals. Studies to evaluate this use may also be worthwhile.

8.2 Limitations

A limitation of the thesis was that all of the included studies were conducted using population samples of cancer patients attending, and cancer doctors practising, at a single site, the Sunshine Coast Cancer Care Service, Nambour Hospital, Queensland, Australia. The validity of results may not necessarily be reflective of cancer patients and doctors from other day cancer centres and further external multiple site studies encompassing a broader population are required to substantiate the results. That said, the study methods were aligned as much as possible to literature recommendations for CAM study survey quality,[230] and study limitations were discussed in the respective discussion sections. For example, a confounding factor for the curative-intent study (Chapter 4), conducted on a sample of cancer patients attending the Sunshine Coast

Cancer Care Service, may not be representative of patients at other sites due to the fact that the Sunshine Coast area recorded the highest percentage of conscientious objection to vaccination in Australia for children aged 5 years,[237] and there is a negative association between vaccination rates with patient care given by CAM providers.[251]

The studies in this thesis followed public hospital patients, the majority of which have no private health insurance. It has been shown that patients with private health insurance are significantly more likely than those without private health insurance to consult CAM practitioners in Australia.[270]

The quality assurance brochure development and post intervention studies (Chapters 6 & 7) were also conducted at the single site (Sunshine Coast Cancer Care Service). This has the limitation that the surveyed cancer patients and cancer doctors may not be representative of patients and cancer doctors at other sites. Further studies at different cancer centres are required to substantiate the positive reception for the educational CAM-with-chemotherapy brochure established in this thesis.

8.3 Future research

People that are commencing curative-intent treatment are arguably the most important demographic of oncology patients. These are the people with the greatest potential to have their cancer eradicated and return to normal life. Therefore, these people deserve continued emphasis in research studies, and continued effort in providing education about the best way to optimise treatment outcomes. The data in this thesis is interesting, and indicates future work with greater participant numbers and at other cancer centres would provide valuable information as to whether they are representative of other sites with different patient and health professional demographics.

The major thesis study (Chapter 4) found that a proportion of cancer patients (13%) being treated with curative-intent chemotherapy were advised not to have chemotherapy adjuvant treatment. This raises the question of what happens to patients, not captured by the study, that accepted this advice and did not present for curative-chemotherapy treatment. A research study to quantify to what extent this

may be occurring and reasons why, would be worthwhile. A longitudinal study of a cohort of these patients may elucidate long term survival difference, whether these patients accepted other forms of conventional interventions such as surgery and/or radiotherapy, whether these patients accept chemotherapy treatment after their cancer has progressed or whether they never accept conventional treatment. The answer to these questions may better prepare conventional cancer providers to provide appropriate support to these patients who are at high risk of diminishing their long-term survival.[65]

8.4 Conclusions

In the absence of strong evidence otherwise, biologically-active CAM should be considered to be contraindicated with curative-intent treatment, as diminishment of chemotherapy dose through biologically-active CAM interaction can correlate with worse disease-free and overall survival outcomes for this cohort of cancer patients.[11-13,112,241]

Cancer patients in this demographic should be informed and dissuaded from taking biologically-active CAM at the same time as adjuvant chemotherapy, particularly as they may be receiving advice to take biologically-active CAM with adjuvant chemotherapy from practitioners, family, friends, and casual acquaintances. A communication bridge is required to disseminate this information because of the additional complication that cancer patients do not necessarily volunteer their CAM consumption, preferring their cancer doctor to initiate discussions regarding CAM use, but most cancer doctors do not initiate CAM discussions with their patients.

An evidence-based CAM-with-chemotherapy patient brochure purpose-designed for use by cancer patients at the time of receiving chemotherapy may provide the communication bridge required to enable cancer care health professionals to educate patients on the potential dangers of biologically-active CAM use with chemotherapy and to provide patients with safe CAM alternatives.

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APPENDIX A

Patient Study Consent Form

Queensland Government

Oncology Trials

Sunshine Coast Cancer Care Centre

Nambour General Hospital

Principal Investigator: **Mr Peter Smith**

Participant Information Sheet and Consent Form

Study Title: Complementary and alternative medicine use by patients receiving chemotherapy

This Participant Information and Consent Form is 4 pages long. Please make sure that you have all the pages.

You are being asked to take part in a research study.

This Participant Information Sheet contains detailed information about the research study. Its purpose is to explain to you as openly and clearly as possible what you would be required to do in the study before you decide whether or not to take part in it.

Please read this Participant Information Sheet carefully. Feel free to ask questions about any information in the document. You may also wish to discuss the study with a relative or friend or your local health worker. Feel free to do this.

Once you understand what the study is about and if you agree to take part in it, you will be asked to sign the Consent Form. By signing the Consent form, you indicate that you understand the information and that you give your consent to participate in the research project.

You will be given a copy of the Participant Information Sheet and Consent form to keep as a record.

This study is being conducted by Cancer Care Services of Nambour General Hospital

1. What is the purpose of this study?

This study aims at finding in the population of cancer patients presenting first time for chemotherapy administration, what complementary approaches to healthcare they are choosing and why they are choosing them.

2. Why have I been asked to participate in this study?

You have been selected to participate in this study because you are being treated with chemotherapy curatively to treat a solid tumour cancer. Knowledge gained through this study may help health professionals working in cancer care to better anticipate and communicate with patients who want to take complementary and alternative medicine (CAM) during chemotherapy treatment. Better understanding of the selection process leading to CAM taken at the same time as chemotherapy may better prepare conventional professionals to ask the right questions and have

appropriate resources to ensure patient safety. Your information is important to us and may help people facing chemotherapy in the future.

3. What if I don't want to take part in this study, or if I want to withdraw later?

Participation in this study is voluntary. It is completely up to you whether or not you wish to participate. Your choice to not participate will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

4. What does this study involve?

If you agree to take part in this study, you will be asked additional questions to the medication history questions routinely asked by the cancer pharmacist in the day cancer unit when you are receiving chemotherapy for the first time. These questions have been designed to find out what complementary medicines you are taking and your reasons for selecting them. Some additional personal questions will also be asked. If you agree to participate in this study, you will be asked to sign the Participant Consent Form.

5. Are there risks to me in taking part in this study?

There are no physical risks involved in this study. Taking part in the study has no effect on your treatment or follow-up which will be decided by you and you're treating doctors according to best standard practice.

Your medical record will be accessed by the researcher involved in the study for further details, however all of your personal details and answers are strictly confidential and will not be revealed to anyone outside the study. Study information will be kept secure at all times and will be destroyed after seven years, according to local hospital policy. Reports of the study will be published, but these will not include details that reveal the identities of patients who took part.

6. What happens if I suffer injury or complications as a result of the study?

It is most unlikely that you will suffer any injury or complications as a result of taking part in this study. By signing the consent form, you have not waived any legal or other right to seek compensation.

7. Will I benefit from the study?

The study aims to further knowledge and to help future people faced with similar decisions in the future, however it may not directly benefit you. You may benefit from having the opportunity to discuss in depth your CAM use and concerns.

8. Will taking part in this study cost me anything?

No.

9. How will my confidentiality be protected?

Study information gathered will not be able to be identified to source. Any identifiable information that is collected about you in connection with this study will remain confidential and will not be disclosed without your permission. This study is to be conducted as part of the requirement of the researcher to achieve a research higher degree through the Graduate School of the University of Queensland. University supervisors will have access to de-identified information gathered in this study.

10. What happens with the results?

If you give permission by signing the Consent Form, results of this study will be used by the researcher to submit a research thesis and may also be published in peer-reviewed journals. In any publication, information will be provided in such a way that you cannot be identified.

12. Further Information or Any Problems

You are encouraged to ask questions at any time during the study interview. If you have any questions about this study, or if you require further information, or you are dissatisfied or unhappy with any aspect of the study, you should first contact the investigator:

The investigator responsible for this study is

Peter Smith (Principal Investigator)

Telephone: 07 5470 6490.

13. Who should I contact if I have concerns about the conduct of this study?

This study has been reviewed and approved by the The Prince Charles Hospital Research, Ethics and Governance Unit, Metro North Health Service District. Should you wish to discuss the study in relation to your rights as a participant, or should you wish to make an independent complaint, you can contact the Executive Officer, The Research, Ethics and Governance Unit, The Prince Charles Hospital, Rode Road, Chermside, Qld 4032 or telephone (07) 3139 4500

Thank you for taking the time to consider being part of this study.

If you wish to take part in this study, please sign the attached consent form.

This information sheet is for you to keep.

Oncology Trials

Sunshine Coast Cancer Care Centre
Nambour General Hospital
Principal Investigator: Mr Peter Smith

Queensland Government

Participant Informed Consent

Pre chemotherapy patient education review

My signature on this consent form means the following:

- I have read and understood the information in this consent form, Version 2. May 21, 2012 (or it has been read to me).
- The study has been fully explained to me and all of my questions have been answered,
- I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or side effect, and of their implications as far as they are currently known by the researchers.
- I understand the purpose of this study and what my participation in it will involve,
- I authorise the use and disclosure of my health information to the parties listed in the confidentiality section of this consent for the purposes described above.
- I understand that the research project will be carried out according to the principles in the National Health & Medical Research Council Statement on Ethical Conduct in Research Involving Humans.
- I give my free and informed consent to take part in the study and agree to the conditions detailed above.
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. If I withdraw from the study I agree to the use of the information collected up to the time of withdrawal.
- I have been informed that The Prince Charles Hospital Research, Ethics and Governance Unit, Metro North Health Service District has approved the study.
- I will receive a copy of this Patient Information Sheet and consent form with my signature on it.
- My signature below indicates that I agree to take part in this study. However my consent does not release the research staff from their responsibilities. I keep all the rights granted by the law.

Printed name of patient	Signature of patient	Date
Printed name of witness	Signature of witness	Date

Statement and signature of person who conducted the informed consent discussion:

I acknowledge that I have explained the information sheet/consent form to the study participant and I believe the patient understood the potential risks and benefits of participation in this trial.

Printed name of Investigator or designated person	Signature	Date

Note: All parties signing the consent form must date their own signature

APPENDIX B

Patient Study Interview Questionnaire

Queensland Government **Nambour General Hospital** **Sunshine Coast Cancer Service** **CAM STUDY QUESTIONNAIRE** **(Interviewer guided)** Researcher: Peter Smith University of Queensland	(Affix Patient Label Here) UR:..... Family name: Given names:..... Date of birth..... Sex: ☐ M ☐ F
Date:	

Socio-demographic information (circle)	
Marital status	married/ live in partner/ (divorced/ separated/ widowed)/ single
Household income ($ gross)	0-30k / 30-59k/ 60-100k/ over100k
Highest educational level	primary/ secondary/ tertiary/ post tertiary
Previous CAM use	No/ yes (routinely/ recent/ rare) what?

Disease characteristics and treatment	
Primary cancer type and stage	
Chemotherapy treatment (curative intent)	
Co- morbidities	
Concurrent conventional cancer treatment	Surgery/ radiotherapy / hormone therapy / other

Complementary and alternative medicines use	
Nutritional supplements (eg Vitamins , minerals, other antioxidants, probiotics)	
Special diet and foods (Gerson diet, "detox", stopping sugar, apricot kernel, shark cartilage)	
Herbal medicines and teas	
Homoeopathy	
Complementary therapies (specified)	
Other (specified)	

Queensland Government **Nambour General Hospital** **Sunshine Coast Cancer Service** **CAM STUDY QUESTIONNAIRE** **(Interviewer guided)** Researcher: Peter Smith University of Queensland	(Affix Patient Label Here) UR:..... Family name:..... Given names:..... Date of birth:..... Sex: ☐ M ☐ F

Date:

Previously communicated CAM use with treating cancer consultant, other cancer health professional or GP?
Yes / No

Why/ why not? (harmless/ not asked/ forgot/ afraid)

Expected benefits from use	Treat unrelated condition / lessen chemotherapy side-effects / treat cancer / improve chemotherapy effectiveness / manage disease symptoms / improve immune system / boost energy / live a healthy lifestyle / feel in control / reduce stress / help sleep / other (specified)?
Do you expect any side-effects from CAM use?	Yes / No
Selection information source	Complementary medicine/therapy practitioner (specific)/ conventional practitioner (specify) / cancer support group/ other patient, friends, family, magazines, books, television, internet, health food store, pharmacy, other (specified).

Specific questions (if applicable):

"Is the person you receive CAM selection advice from in favour of you receiving chemotherapy?" Yes / No

"Would you have liked to receive from us specific information on what complementary medicines are safe to use with chemotherapy ? Yes / No

If yes :

- From whom? Consultant/ Nurse/ Pharmacist/ GP, other (specify)
- When would this be most useful? Initial consultation/ Other time
- What? Referenced guide / Verbal advice / Other? (specify)

APPENDIX C

Patient Study Medication History Form

Queensland Government
Queensland Health

Sunshine Coast Health Service District
Nambour General Hospital
Sunshine Coast Cancer Service

MEDICATION HISTORY

(Affix Patient Label Here)

UR:.....

Family name:.....

Given names:.....

Date of birth:..... Sex: ☐ M ☐ F

Date:

Source of History: ☐ Patient ☐ Carer ☐ Other:

ADVERSE DRUG EVENT or ALLERGY Patient states they have an allergy ☐ **YES** ☐ **NO**

Drug / Food	Reaction	When

PRESCRIPTION MEDICATIONS (prescribed prior to Admission)

Generic Name	Dose and Frequency	When Started	Indication per patient

OVER THE COUNTER MEDICATIONS
Does the patient use any medications bought from a chemist, health food store or supermarket?

Generic Name	Dose and Frequency	When Started	Indication per patient

Signature:	Name:	Designation:

APPENDIX D

TPCH Patient Study Ethics Approvals (HREC/12/QPCH/33)

Queensland Government

Mr Peter Smith
Sunshine Coast Cancer Care Services
Cancer Services Pharmacy
Level 2
Nambour General Hospital
NAMBOUR QLD 4560

Queensland Health
Human Research Ethics Committee
The Prince Charles Hospital
Metro North Health Service District
Administration Building, Lower Ground
Rode Road, Chermside QLD 4032

Executive Officer Research & Ethics Ph: (07) 3139 4500
Office Ph: (07) 3139 4691
Our Ref: PI/JI/ Low Risk Approval

13 March 2012

Dear Mr Smith,

Re: HREC/12/QPCH/33: What complementary and alternative medicine is taken by patients with solid tumour malignancies receiving for the first time curative intent chemotherapy in a hospital day unit and what factors influence selection at that time? P. Smith

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed your submission and upon recommendation, the Chair has granted final approval for your low risk project.

I am pleased to advise that the Human Research Ethics Committee has granted approval of this research project. The documents reviewed and approved include:

Document	Version	Date
Low Risk Application		
Protocol	1	17 February 2012
Participant Information Sheet & Consent Form (Nambour)	1	7 February 2012

Approval of this project is subject to the same confidentiality and privacy requirements as apply to other research projects and research subjects are not recognisable in publications or oral presentations.

You are reminded that this letter constitutes ethical approval only. **You must not commence this research project at a site until separate authorisation from the District CEO or Delegate of that site has been obtained.**

A copy of this approval must be submitted to the District Research Governance Officer/Delegated Personnel with a completed Site Specific Assessment (SSA) Form for authorisation from the CEO or Delegate to conduct this research at The Nambour Hospital.

Please complete the Commencement Form before starting your study and return to the office of the Human Research Ethics Committee. http://www.health.qld.gov.au/tpch/documents/form_notification.dot

If you intend to publish the results of your work, it is advisable to ascertain from prospective journal editor/s the actual requirements for publication e.g. some journals may require full ethical review of all studies. When results are published, appropriate acknowledgment of the hospital should be included in the article. Please forward copies of all publications resulting from the study for inclusion in the Internet website list.

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your research endeavour.

Yours truly,

Dr Russell Denman
Chair
HUMAN RESEARCH ETHICS COMMITTEE
METRO NORTH HEALTH SERVICE DISTRICT

Queensland Government

Queensland Health

Human Research Ethics Committee
The Prince Charles Hospital
Metro North Health Service District
Administration Building, Lower Ground
Rode Road, Chermside QLD 4032

Enquiries to: Jacqui_Hayward@health.qld.gov.au
Philip_Lee@health.qld.gov.au
Office Ph: (07) 3139 4691
(07) 3139 4500
Our Ref: PI/JI/Approval Amendments

Mr Peter Smith
Cancer Care Centre
Level 2, Block 1
Nambour General Hospital
Hospital Road
NAMBOUR QLD 4560

24 May 2012

Dear Mr Smith,

Re: **HREC/12/QPCH/33: What complementary and alternative medicine is taken by patients with solid tumour malignancies receiving for the first time curative intent chemotherapy in a hospital day unit and what factors influence selection at that time? P. Smith**

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed the amendments submitted 22 May 2012 and upon recommendation, the Chair has granted approval for the following:

- Participant Information Sheet & Consent Form – Version 2, dated 21 May 2012

Sites included under this approval are:

No.	Site
1	Nambour Hospital

Patient information collected and distributed as part of the previously approved research has been approved in accordance with Section 62 of the Health Services Act and the recent amendments to the Public Health Act Sections 282 and 284. Any change to the collection and or distribution will need to be reviewed by the HREC.

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your research endeavour.

Yours truly,

Philip Lee, MBA (UQ); BAppSc (QUT); FRCNA; AFAIM
Executive Officer – Research, Ethics and Governance Unit
Email: Philip_Lee@health.qld.gov.au

APPENDIX E

UQ Patient Study Ethics Approvals (2012/07)

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

School of Pharmacy

12 April 2012

Mr Peter Smith
41 Kestrel Crescent
Peregian Beach QLD 4573

Dear Peter,

Ethics Committee Approval – (2012/07)
'What complementary and alternative medicine is taken by patients with solid tumour malignancies receiving for the first time curative intent chemotherapy in a hospital day unit and what factors influence selection at that time?'

I am pleased to advise that the School of Pharmacy Ethics Committee has given approval to your application for the above project.

However, should any deviation from the approved research protocol occur please inform the Committee as it may be necessary to resubmit an amended protocol for ethical approval.

The Committee would like to wish you every success for the outcome of your project.

If you have any further queries please do not hesitate to contact me.

Yours sincerely,

Vanessa King
Secretary
School of Pharmacy
Ethics Committee

School of Pharmacy
Pharmacy Australia Centre of Excellence
The University of Queensland
20 Cornwall St
Woolloongabba QLD 4102 Australia
T +61 7 3346 1900
F +61 7 3346 1999
E enquiries@pharmacy.uq.edu.au
W www.uq.edu.au/pharmacy

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

School of Pharmacy

5th June 2012

Mr Peter Smith
41 Kestrel Crescent
Peregian Beach QLD 4573

Dear Peter,

Ethics Committee Approval to Amendment – (2012/07)
'What complementary and alternative medicine is taken by patients with solid tumour malignancies receiving for the first time curative intent chemotherapy in a hospital day unit and what factors influence selection at that time?'

I am pleased to advise that the School of Pharmacy Ethics Committee has given approval to your amended Trial consent form.

However, should any deviation from the approved research protocol occur please inform the Committee as it may be necessary to resubmit an amended protocol for ethical approval.

The Committee would like to wish you every success for the outcome of your project.

If you have any further queries please do not hesitate to contact me.

Yours sincerely,

Nadine Savage

Nadine Savage
Secretary
School of Pharmacy
Ethics Committee

School of Pharmacy
Pharmacy Australia Centre of Excellence
The University of Queensland

20 Cornwall Street
Woolloongabba Qld 4102 Australia

T +61 7 3346 1900
F +61 7 3346 1999

E enquiries@pharmacy.uq.edu.au
W www.uq.edu.au/pharmacy

APPENDIX F

SCHHS Patient Study Governance Approval (SSA/12/QNB/67)

Queensland Government

Enquiries Megan Rutter
Telephone 07 5370 3790
Facsimile 07 5470 5482
Email SC-Research-Governance @health.qld.gov.au
File Ref HREC/12/QPCH/33

Mr Peter Smith
Oncology Pharmacy
Sunshine Coast Cancer Services
Nambour General Hospital
Nambour QLD 4560

Dear Mr Smith

HREC reference number: HREC/12/QPCH/33
SSA reference number: SSA/12/QNB/67
Project title: What complementary and alternative medicine is taken by patients with solid tumour malignancies receiving for the first time curative intent chemotherapy in a hospital day unit and what factors influence selection at that time?

Thank you for submitting an application for Sunshine Coast Hospital and Health Service authorisation of the above project. I am pleased to inform you that authorisation has been granted for this study to take place at the following site(s): Nambour General Hospital.

Authorisation to commence the above research has been provided on the basis of the following documents:

Description	Version	Document Date
Letter to RGO		18-Apr-12
Low Risk Ethics and SSA Form		
Prince Charles HREC approval	Initial Approval	13-Mar-12
Prince Charles HREC approval	Amendment to PICF	24-May-12
UQ School of Pharmacy Ethics approval	Initial approval	12-Apr-12
UQ School of Pharmacy Ethics approval	Amendment to PICF	5-Jun-12
Research Plan	1	17-Feb-12
Nambour General Hospital PICF	2	21-May-12
Study Questionnaire	1	17-Feb-11
Research Agreement		

The following conditions apply to this research proposal. These are additional to those conditions imposed by the Human Research Ethics Committee (HREC) that granted ethical approval:

1. Annual Reports must be supplied to the Prince Charles Hospital HREC and the Sunshine Coast Research Governance Officer (RGO) annually from the date of HREC approval.
2. A Final Report must be supplied to the Prince Charles Hospital HREC and the Sunshine Coast Research Governance Officer (RGO) on completion of the study.
3. Proposed amendments to the research protocol or conduct of the research which may affect the ethical acceptability of the project are to be submitted to the HREC for review. A copy of the HREC approval/rejection letter along with the proposed amendments must be submitted to the RGO.

4. Proposed amendments to the research protocol or conduct of the research which only affects the ongoing site acceptability of the project are to be submitted to the RGO.
5. A proposed amendment to the research protocol or conduct of the research which may affect both the going ethical acceptability of the project and the site acceptability of the project are to be submitted firstly to the HREC for review and then to the research governance officer after a HREC decision is made.

Sunshine Coast Hospital and Health Service authorisation for this research is valid for the period of the HREC approval. It is the responsibility of the researcher to ensure they maintain current and valid HREC approval and Research Governance authorisation.

Yours sincerely

J Hanson

Jackie Hanson
Acting Health Service Chief Executive
Sunshine Coast Hospital and Health Service

14/12/12

APPENDIX G

Draft Patient Brochure

What complementary and alternative medicine (CAM) can I safely use with chemotherapy?

Evidence-based information for patients

Peter J Smith,[1,2] Alexandra Clavarino,[1] Jeremy Long[2] and Kathryn J Steadman[1]

[1]University of Queensland, Brisbane, Australia
[2]Sunshine Coast Cancer Care Services, Nambour, Australia

Version 1, 2014

Introduction

This brochure is designed to advise you on what we currently know about complementary and alternative medicine (CAM) use at the time of receiving chemotherapy. It does not cover CAM use at other times, for example, when you have completed conventional treatment. It is also not in any way a criticism of all CAM use, just a summation of current evidence-based studies on CAM effectiveness and assured safety at this time.

This brochure will provide you with evidence-based information on which CAM we know is safe for you to use, if you wish, during treatment with chemotherapy.

What is CAM?

Complementary and alternative medicine (CAM) are products and treatments which are not widely used by conventional healthcare professionals.[2] CAM that is absorbed into the bloodstream, such as herbs and vitamin supplements, may interfere with chemotherapy effectiveness.[11,12]

Herbs and vitamin supplements are absorbed into the bloodstream and may interfere with chemotherapy effectiveness

Mind-body CAM

Mind-body CAM such as massage, meditation, music, imagery, hypnosis, self-expression, mild exercise and acupuncture have established evidence and are able to be used safely with standard treatment. Mind-body therapies should be your first consideration when looking for safe, complementary cancer care. (Table 1)

Mind-body therapies are safe and effective complementary treatments you can use while receiving chemotherapy.

Table 1.

***Safe, evidence- based mind-body CAM* that *may help during chemotherapy treatment*[17]**

**** Acupuncture, hypnosis and massage should be administered by specially trained practitioners***

Mind-body therapy CAM	Supportive care use
Acupuncture*	• decreases acute vomiting caused by chemotherapy
Hypnosis*	• decreases nausea and vomiting caused by chemotherapy
Imagery and relaxation (body relaxation combined with visualisation e.g. imagining immune cells as powerful medieval knights, or big brooms, dispatching cancer cells)	• positively modulates immune functioning during treatment
Massage*	• decreases nausea and vomiting caused by chemotherapy • reflexology (foot massage) decreases anxiety during treatment
Meditation (combines relaxation with self-awareness, which brings the person into the moment, free from anxiety concerning the past or future)	• alters immune patterns by decreasing stress • decreases anxiety and depression
Music	• reduces anxiety
Self-expression (includes written or verbal expression, artwork, humour and movement)	• decreases dark feelings and improves outlook
Mild exercise (includes yoga)	• reduces fatigue and enhances life satisfaction

***Other mind-body CAM that is safe to use during chemotherapy treatment**:*

Aromatherapy (inhaled), Bowen therapy, Qi gong, Reiki, Tai Chi, Therapeutic touch

Evidence to use CAM

To treat cancer

There is not yet enough conclusive evidence to recommend to you any CAM to treat cancer. Delaying conventional treatment to use CAM alone to try and treat cancer may potentially sacrifice years of your life, particularly if your cancer is at an early stage.[65]

For chemotherapy support

Apart from mind-body therapies (Table 1) and ginger for the treatment of nausea, it is very difficult to find consistent, high quality studies which show beyond doubt that a CAM is effective, is safe, and is able to be recommended to you when you are receiving chemotherapy. Probiotics have shown some benefit to lessen diarrhoea, which can be a side effect of particular chemotherapy and fish oil has helped some lung cancer patients resist weight loss (Table 2).

Table 2.

Oral CAM that may help during chemotherapy treatment[17]

Oral CAM	Supportive care use
Ginger	• reduces nausea caused by chemotherapy
Probiotics/ Yoghurt	• decreased diarrhoea caused by chemotherapy Caution Probiotics are normally well tolerated; however, there have been rare cases of very ill patients receiving chemotherapy developing serious probiotic-caused infections
Fish oil supplements	• fish oil taken daily may provide benefit to patients with lung cancer through maintenance of weight during chemotherapy administration

I am already using CAM to treat something else

You may already be taking herbal medicines or vitamin supplements regularly to treat existing conditions, or occasionally for example to treat cold symptoms. It is important that you declare this CAM use, as there may be a chance of interaction depending on the chemotherapy you are receiving.[7]

How may CAM interfere with chemotherapy?

Practitioners carefully calculate chemotherapy doses individually for you, as accuracy is crucial in ensuring that you get the maximum anticancer action with the least side effects possible. CAM such as herbal medicines, which are absorbed into the bloodstream, may potentially interfere with your chemotherapy in a way that lessens the anticancer effect or gives you more side effects by making the chemotherapy more toxic to you.[11,12] (Table 3)

Potential interactions with CAM may make chemotherapy more toxic to you, or may lessen the anticancer effect of the chemotherapy.

Antioxidants: can I take them?

The use of supplemental antioxidants by cancer patients receiving chemotherapy remains controversial. Beneficial effects of taking antioxidant supplements to reduce side effects may be at the cost of lessening the chemotherapy anticancer effect, depending on which chemotherapy you are receiving.[114] (Table 3) Until further, definitive research is done, caution is advised when taking antioxidant supplements at the time of receiving chemotherapy.[73]

Beneficial effects of taking antioxidants to reduce side effects may be at the cost of lessening the chemotherapy anticancer effect

Fortunately, eating antioxidant-containing foods in your normal diet is safe with chemotherapy.[114]

Antioxidant-containing foods in your normal diet do not achieve high enough levels to interact with chemotherapy.

Table 3.
CAM and potential interactions with chemotherapy [271]

CAM	Interaction with chemotherapy	Explanation
Antioxidant supplements	Interaction likely with particular chemotherapy Diminishes radiotherapy effectiveness	Concern that antioxidant supplements may protect cancer cells as well as normal cells
Herbs, Chinese herbs, Medical herbal teas	It has been estimated that herbal interactions are responsible for a substantial number of unexpected toxicities of chemotherapy and possible under treatment seen in cancer patients Chinese herbal mixtures often contain many different plant extracts which are highly biologically-active, increasing chance of interaction	There is indirect evidence for both positive and negative effects of herbal use with chemotherapy; however, currently, there is not enough information available about herb-chemotherapy interactions to make definite recommendations
Medicinal mushrooms (*Coriolus versicolor* "PSK", *Ganoderma lucidum* "Reishi")	Interaction unlikely with most chemotherapy	No reported negative interactions
Trace mineral supplements	Interaction unlikely with very small doses of minerals	No information or valid explanations available for potential negative interactions
Homeopathy (also Bach flower remedies, bush flower essences, Schuessler's tissue salts)	Interaction unlikely	Homeopathic products are so diluted that there is little chance of interaction.

I still want to take CAM

If you decide to take CAM at the time you are receiving chemotherapy, for example if you have an advanced cancer, and are willing to accept potential interaction risk, it is still very important that you declare this use to your cancer specialist or pharmacist for documentation, to enable the best care to be given to you.

Require more information?

National Cancer Institute
Complementary and alternative medicine in cancer treatment:
http://www.cancer.gov/cancertopics/pdq/cam/cam-cancer-treatment/patient
Thinking about complementary and alternative medicine: A guide for people with cancer
http://www.cancer.gov/cancertopics/cam/thinking-about-CAM

Memorial Sloan Kettering Cancer Center
Complementary therapies to ease the way during cancer treatment and recovery
http://www.mskcc.org/cancer-care/patient-education/resources/complementary-therapies-ease-way-during-treatment-and-recovery

Cancer Council Australia
Complementary and alternative therapies:
http://www.cancer.org.au/about-cancer/treatment/complementary-therapies-and-cancer.html

APPENDIX H

SCHHS Queensland Government Published Patient Brochure

What complementary and alternative medicine (CAM) can I safely use with chemotherapy?

Evidence-based information for patients

Version 2 Jan 2016

Peter J Smith,[1,2] Alexandra Clavarino,[1] Jeremy Long[2] and Kathryn J Steadman[1]
[1]The University of Queensland, Brisbane, Australia
[2]Sunshine Coast Cancer Care Services, Nambour, Australia

Sunshine Coast
Hospital and Health Service
Exceptional people. Exceptional healthcare.

Queensland
Government

Introduction

This booklet is designed to advise you about the use of complementary and alternative medicine (CAM) when receiving chemotherapy. It does not cover CAM use at other times, for example, when you have completed conventional treatment. This is a summary of current, evidence-based studies on CAM effectiveness and safety. It is not a criticism of CAM use.

What is CAM?

Complementary and alternative medicine (CAM) are products and treatments which are not widely used by conventional healthcare professionals.[1] CAM that is absorbed into the bloodstream, such as herbs and vitamin supplements, may interfere with chemotherapy effectiveness.[2,3]

Mind-body CAM

Mind-body CAM such as massage, meditation, music, imagery, hypnosis, self-expression, mild exercise and acupuncture have established evidence and are able to be used safely with standard treatment. Mind-body therapies should be your first consideration when looking for safe, complementary cancer care. (Table 1)

This booklet will provide you with evidence-based information on which CAM we know is safe for you to use, if you wish, during treatment with chemotherapy.

Herbs and vitamin supplements are absorbed into the bloodstream and may interfere with chemotherapy effectiveness.

Mind-body therapies are safe and effective complementary treatments you can use while receiving chemotherapy.

Table 1.

Safe, evidence-based mind-body CAM that may help during chemotherapy treatment[4]

* Acupuncture, hypnosis and massage should be administered by specially trained practitioners

Mind-body therapy CAM	Supportive care use
Acupuncture*	• decreases acute vomiting caused by chemotherapy.
Hypnosis*	• decreases nausea and vomiting caused by chemotherapy.
Imagery and relaxation (body relaxation combined with visualisation e.g. imagining warm sun melting away cancer cells)	• boosts immune functioning during treatment.
Massage*	• decreases nausea and vomiting caused by chemotherapy • reflexology (foot massage) decreases anxiety during treatment.
Meditation (combines relaxation with self-awareness, which brings the person into the moment, free from anxiety concerning the past or future)	• alters immune patterns by decreasing stress • decreases anxiety and depression.
Music	• reduces anxiety.
Self-expression (includes written or verbal expression, artwork, humour and movement)	• decreases dark feelings and improves outlook.
Mild exercise (includes yoga)	• reduces fatigue and promotes wellbeing.

Other mind-body CAM that is safe to use during chemotherapy treatment: aromatherapy (inhaled), bowen therapy, Qigong, reiki, tai chi, therapeutic touch

Is there evidence to use CAM?

To treat cancer
There is not yet enough conclusive evidence to recommend to you any CAM to treat cancer. Delaying conventional treatment to use CAM alone to try and treat cancer may potentially sacrifice years of your life, particularly if you are being treated with curative intent.[5]

For chemotherapy support
Apart from mind-body therapies (Table 1), it is very difficult to find consistent, high quality studies which show beyond doubt that a CAM is effective, is safe, and is able to be recommended to you when you are receiving chemotherapy. Ginger is well known to be a useful treatment for nausea, including nausea caused by chemotherapy, and probiotics may reduce diarrhoea caused by some chemotherapy treatments (Table 2).

Table 2

Oral CAM that may help during chemotherapy treatment[4].

Oral CAM	Supportive care use
Ginger	• may reduce nausea caused by chemotherapy.
Probiotics/yoghurt	• may decrease diarrhoea caused by chemotherapy. **Caution** Probiotics are normally well tolerated; however, there have been rare cases of very ill patients receiving chemotherapy developing serious probiotic-caused infections

Already using CAM to treat something else?

You may already be taking herbal medicines or vitamin supplements regularly to treat existing conditions, or occasionally for example to treat cold symptoms. It is important that you declare this CAM use, as there may be a chance of interaction depending on the chemotherapy you are receiving.[6]

How may CAM interfere with chemotherapy?

Practitioners carefully calculate chemotherapy doses individually for you, as accuracy is crucial in ensuring that you get the maximum anticancer action with the least side effects possible. CAM that are absorbed into the bloodstream, such as herbal medicines, may potentially interfere with your chemotherapy in a way that lessens the anticancer effect or gives you more side effects by making the chemotherapy more toxic to you[2,3] (Table 3).

Potential interactions with CAM may make chemotherapy more toxic to you, or may lessen the anticancer effect of the chemotherapy.

Antioxidants: can I take them?

The use of supplemental antioxidants by cancer patients receiving chemotherapy remains controversial. Beneficial effects of taking antioxidant supplements to reduce side effects may be at the cost of lessening the chemotherapy anticancer effect, depending on which chemotherapy you are receiving[7] (Table 3). Until further definitive research is done, caution is advised when taking antioxidant supplements at the time of receiving chemotherapy.[8]

Beneficial effects of taking antioxidants to reduce side effects may be at the cost of lessening the chemotherapy anticancer effect.

Fortunately, eating antioxidant-containing foods in your normal diet is safe with chemotherapy.[7]

Antioxidant-containing foods in your normal diet do not achieve high enough levels to interact with chemotherapy.

Table 3.

CAM and potential interactions with chemotherapy[2,3,7,9,10]

CAM	Interaction with chemotherapy	Explanation
Antioxidant supplements (vitamins A, C and E, CoQ10 and others).	Interaction likely with particular chemotherapy. Diminishes radiotherapy effectiveness.	Concern that antioxidant supplements may protect cancer cells as well as normal cells.
Herbs, Chinese herbs, medical herbal teas.	It has been estimated that herbal interactions are responsible for a substantial number of unexpected toxicities of chemotherapy and possible under treatment seen in cancer patients. Chinese herbal mixtures often contain many different plant extracts which are highly biologically-active, increasing chance of interaction.	There is indirect evidence for both positive and negative effects of herbal use with chemotherapy; however, currently, there is not enough information available about herb-chemotherapy interactions to make definite recommendations.
Medicinal mushrooms (Coriolus versicolor "PSK", Ganoderma lucidum "Reishi").	Interaction unlikely with most chemotherapy.	No reported negative interactions.
Trace mineral supplements.	Interaction unlikely with very small doses of minerals.	No information or valid explanations available for potential negative interactions.
Homeopathy (also Bach flower remedies, Australian bush flower essences, Schuessler's tissue salts).	Interaction unlikely.	Homeopathic products are so diluted that there is little chance of interaction.

I still want to take CAM

If you decide to take CAM at the time you are receiving chemotherapy, for example if you have an advanced cancer and are willing to accept potential interaction risk, it is still very important that you tell your cancer specialist or pharmacist for documentation, to enable the best care to be given to you.

Require more information?

National Cancer Institute
Complementary and alternative medicine in cancer treatment:
http://www.cancer.gov/cancertopics/pdq/cam/cam-cancer-treatment/patient

Thinking about CAM: A guide for people with cancer
http://www.cancer.gov/cancertopics/cam/thinking-about-CAM

Memorial Sloan-Kettering Cancer Center
Complementary therapies to ease the way during cancer treatment and recovery:
http://www.mskcc.org/cancer-care/patient-education/resources/complementary-therapies-ease-way-during-treatment-and-recovery

Cancer Council Australia
Complementary and alternative therapies:
http://www.cancer.org.au/about-cancer/treatment/complementary-therapies-and-cancer.html

References

1. Zollman C, Vickers A. ABC of complementary medicine. Complementary medicine and the patient. *BMJ* Dec 4 1999;319(7223):1486-1489.
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3. Meijerman I, Beijnen JH, Schellens JH. Herb-drug interactions in oncology: focus on mechanisms of induction. *Oncologist.* Jul-Aug 2006;11(7):742-752.
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Standard 1: Governance for Safety and Quality in Health Service Organisations
Involves setting direction, making policy and strategy decisions, overseeing and monitoring organisational performance and ensuring overall accountability for a service.

Standard 2: Partnering with Consumers
Consumers and/or carers provided feedback on this patient information.

Standard 4: Medication Safety
Reduction in the occurrence of medication incidents, and improvement to the safety and quality of medicine use.

Standard 11: Service Delivery
Patients and the community have access to safe, high quality healthcare services that are appropriate, effective and meet their needs.

Standard 12: Service Delivery
To ensure high quality care is delivered to consumers/patients through the care continuum.

APPENDIX I

Brochure Evaluation Study Patient Consumer Feedback Form

Sunshine Coast Hospital and Health Service

Consumer testing feedback form

Sunshine Coast Hospital and Health Services (SCHHS) have developed a patient/carer brochure:

to provide information about:

We invite your participation in providing feedback on the design and content of this resource, to ensure we are providing the best information we can to our patients and their carers and families. Your details will not be collected or used for any other purposes than providing feedback on this resource.

Thank you for your involvement!

Title: Surname: Given Name:

Postal Address:

State: Post Code: Email Address:

Home Phone: Mobile Phone:

Information about you

- ☐ Under 18
- ☐ 18 - 24
- ☐ 25 - 39
- ☐ 40 - 64
- ☐ 65 - 74
- ☐ 75+

- ☐ Male
- ☐ Female

- ☐ I am a patient
- ☐ I am a family member or friend of a patient
- ☐ I am a carer
- ☐ I am a Health care professional
- ☐ Other, please specify:

☐ I am a person with a disability	Please specify:
☐ I identify as an Aboriginal and/or Torres Strait Islander	Please specify:
☐ I identify as a member of a cultural or ethnic group	Please specify:
☐ I am a person from a Non-English Speaking Background	Please specify:
☐ I am a member of a human service community service/ or welfare organisation	Please specify:
☐ I am a member of an advocacy or rights based organisation	Please specify:

- ☐ I left school before completing year 10
- ☐ I have completed year 10
- ☐ I have completed year 12
- ☐ I have completed tertiary education — Please specify: ____
- ☐ I have completed postgraduate education — Please specify: ____

What geographical areas do you live in?

- ☐ Gympie Region
- ☐ Sunshine Coast Hinterland (e.g. Maleny, Montville and surrounding areas)
- ☐ Sunshine Coast South (e.g. Caloundra, Kawana and surrounding areas)
- ☐ Sunshine Coast North (e.g. Noosa and surrounding areas)
- ☐ Other, please specify: ____

Publication Feedback

1. Did you find the information clear, easy to read and understand? YES ☐ NO ☐

Any comments: ____

2. Was there enough information to answer your questions? YES ☐ NO ☐

If not, what other information would be useful (please specify): ____

3. What were the main messages?

Please specify: ____

4. What do you feel you should do as a result of reading this resource?

Please specify: ____

Sunshine Coast Hospital and Health Service

5. Did the information explain medical terms well?	YES ☐	NO ☐
6. Do you believe this information is relevant to you?	YES ☐	NO ☐
Any Comments:		
7. Is the content culturally sensitive and appropriate?	YES ☐	NO ☐
If no, please specify why:		
8. Is the design appropriate and appealing?	YES ☐	NO ☐
9. Is the design clear, uncluttered, and easy to follow?	YES ☐	NO ☐
10. Is the print large and clear enough?	YES ☐	NO ☐
11. Did the photos and illustrations help you understand the information?	YES ☐	NO ☐

12. Are there any other comments or suggestions that you would like to make?

APPENDIX J

Brochure Evaluation Study Prescriber Feedback Form

Brochure Feedback Form

- I am a (please tick):

	Oncologist		Haematologist		Rotational registrar
	Training oncology registrar		Training haematology registrar		Other (please clarify below)

- Do you think there is a need for this brochure? (please tick)

  ☐ yes
  ☐ no

- Would you recommend this brochure to your patients?

  ☐ yes
  ☐ no (skip to feedback at bottom)

- Which patients receiving chemotherapy would you recommend this brochure to? (tick more than one answer if required)

  ☐ all patients
  ☐ patients /carers who ask about CAM , or are using CAM
  ☐ only early stage/ curative intent patients
  ☐ other (specify)

- Who should give this brochure to the patient? (tick more than one answer if required)

  ☐ treating consultant/ registrar
  ☐ nurse at clinic education
  ☐ other cancer care professional (specify):
  ☐ general practitioner
  ☐ other (specify)

- Please add any other feedback/suggestions/ criticisms:

Please return this form to Peter Smith, Cancer Care Pharmacy, Nambour General Hospital. peter.smith@health.qld.gov.au

APPENDIX K

Brochure Post Evaluation Prescriber Feedback Form

CAM-chemotherapy brochure post intervention prescriber survey

1. I am a (please tick):

	Oncologist		Haematologist	
	Oncology registrar		Haematology registrar	

2. Do you think there is a need for this brochure? (please tick)

☐ yes
☐ no

3. Do you recommend this brochure to your patients?

☐ yes
☐ no

4. Do you think this brochure makes it easier for you to discuss CAM with your patients?

☐ yes
☐ no

Please comment:

5. Has the brochure saved you time during patient consultations?

☐ yes
☐ no

Please comment:

6. Which patients do you recommend this brochure to?
(tick more than one answer if required)

- ☐ all patients receiving chemotherapy
- ☐ patients you know are using CAM
- ☐ patients /carers who ask about CAM
- ☐ only early stage/ curative intent patients
- ☐ I wouldn't recommend it to any patients
- ☐ other (specify)

7. Who should be able to give the brochure to your patients?
(tick more than one answer if required)

- ☐ treating consultant/ registrar
- ☐ nurse at clinic education
- ☐ any nurse in cancer care day unit
- ☐ cancer pharmacist
- ☐ any health professional in cancer care day unit
- ☐ displayed in the day unit waiting room (for anyone to take)
- ☐ GP
- ☐ other (specify)

8. Who would you <u>prefer</u> to give the brochure to your patients?
(only one answer please)

- ☐ treating consultant/ registrar
- ☐ nurse at clinic education
- ☐ any nurse in cancer care day unit
- ☐ cancer pharmacist
- ☐ any health professional in cancer care day unit
- ☐ displayed in the day unit waiting room (for anyone to take)
- ☐ GP
- ☐ Other (specify)

Please add any other feedback/suggested additions or omissions for the next edition:

Please return this form to Peter Smith, Cancer Care Pharmacy, Nambour General Hospital. peter.smith@health.qld.gov.au

APPENDIX L

TPCH Patient Brochure Evaluation Study Ethics Waiver (HREC14QPCH199)

Enquiries to: R&ETPCH@health.qld.gov.au
Office Ph: Anne.Carle@health.qld.gov.au
(07) 3139 4198
Our Ref: (07) 3139 4500
AC/JI/Exemption

Queensland Government

15 September 2014

Human Research Ethics Committee
Metro North Hospital and Health Service
The Prince Charles Hospital
Building 14
Rode Road, Chermside QLD 4032

Mr Peter Smith
Pharmacist
Cancer Care Services
Sunshine Coast Hospital and Health Service
Nambour Hospital
P.O. Box 547
Nambour QLD 4560

Dear Mr Smith

Re: **HREC/14/QPCH/199: Evaluation of a Patient CAM-with-chemotherapy Education Brochure**

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed the above project submitted on 15 Septyember

This is to confirm that this project meets the National Statement definition of a project that is exempt from full ethical review on the basis that this is an audit/quality assurance project.

The documents reviewed and approved for the above mentioned project include:

- Proposal submitted on 15 September 2014.
- Evidence Based Information for Patients
- Brochure Feedback Form
- Consumer Testing Feedback Form

This exemption is subject to the following conditions:

- The project must be carried out in accordance with the National Statement on Ethical Conduct in Human Research 2007.

- If the results of your project are to be published, please include an appropriate acknowledgement of the relevant department/s who have

supported this project.

- The HREC may audit the conduct of any project reviewed under NHMRC guidelines. This may include consultation with the Principal Investigator and/or a visit to the site/s by members of the HREC or their delegate.

- Please advise the Human Research Ethics Committee of the date you intend to commence the project.
(http://www.health.qld.gov.au/tpch/documents/form_notification.dot)

On behalf of the Human Research Ethics Committee, I would like to wish you every success with your project.

Yours sincerely

Anne Carle
A/-Executive Officer
Research, Ethics and Governance Unit

APPENDIX M

TPCH Brochure Post Evaluation Study Ethics Exemption (HREC/15/QPCH/93)

Enquiries to: R&ETPCH@health.qld.gov.au
Office Ph: Anne.Carle@health.qld.gov.au
(07) 3139 4198
Our Ref: (07) 3139 4500
AC/ji/Exemption

Queensland Government

14 April 2015

Human Research Ethics Committee
Metro North Hospital and Health Service
The Prince Charles Hospital
Building 14
Rode Road, Chermside QLD 4032

Dr Peter Smith
Pharmacist
Cancer Care Services
Sunshine Coast Hospital and Health Services
Nambour Hospital
PO Box 547
Nambour QLD 4560

Dear Dr Smith

Re: **HREC/15/QPCH/93: Post intervention survey of a patient CAM-with-chemotherapy educational brochure**

I am pleased to advise that The Prince Charles Hospital Human Research Ethics Committee reviewed the above project submitted on 11 March 2015.

This is to confirm that this project meets the National Statement definition of a project that is exempt from full ethical review on the basis that this is an audit/quality assurance project.

The documents reviewed and approved for the above mentioned project include:

- Proposal supplied on 11 March 2015
- Consumer Testing Feedback Form
- CAM-Chemotherapy Brochure Post Intervention Survey
- Information Brochure

This exemption is subject to the following conditions:

- The project must be carried out in accordance with the National Statement on Ethical Conduct in Human Research 2007.

- Please provide an annual report on the outcomes of this project.

APPENDIX N

UQ Brochure Post Evaluation Study Ethics Exemption (2015/10)

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

School of Pharmacy

21st July 2015

Mr Peter Smith
Cancer Care Services
Sunshine Coast Hospital and Health Services
Nambour Hospital
POBox547
Nambour QLD 4560

Dear Peter,

Ethics Committee Approval – (2015/10)
'Post intervention survey of a patient CAM-with-Chemotherapy educational brochure (HREC/15/QPCH/93)'

The School of Pharmacy Ethics Committee notes and recognises the ethics exemption you have received from The Prince Charles Hospital HREC for your project.

Should any deviation from the approved research protocol occur please inform the Committee as it may be necessary to submit an amended protocol for ethical approval.

The Committee would like to wish you every success for the outcome of your project.

If you have any further queries please do not hesitate to contact me.

Yours sincerely,

Vanessa King

Secretary
School of Pharmacy
Ethics Committee

School of Pharmacy
Pharmacy Australia Centre of Excellence
The University of Queensland

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